Exhibit 25

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

IN RE: ACETAMINOPHEN – ASD-ADHD PRODUCTS LIABILITY LITIGATION	) MDL No. 3043) Case No. 1:22-md-03043-DLC
THIS DOCUMENT RELATES TO: All Cases, 1:22-md-03043	) JUDGE DENISE COTE

WEDNESDAY, SEPTEMBER 6, 2023

CONFIDENTIAL - PURSUANT TO PROTECTIVE ORDER

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Videotaped deposition of Jennifer Pinto-Martin, Ph.D., MPH, held at the offices of Barnes & Thornburg, 1717 Arch Street, Suite 4900, Philadelphia, Pennsylvania, commencing at 8:42 a.m. Eastern, on the above date, before Carrie A. Campbell, Registered Diplomate Reporter, Certified Realtime Reporter, Illinois, California & Texas Certified Shorthand Reporter, Missouri, Kansas, Louisiana & New Jersey Certified Court Reporter.

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EXHIBITS

VIDEOGRAPHER: We are now on the record. My name is Brian McGee. I'm a videographer for Golkow Litigation Services.

Today's date is September 6, 2023, and the time is 8:42 a.m.

This video deposition is being held in Philadelphia, PA, in the matter of Acetaminophen (Tylenol) ASD/ADHD Products Liability Litigation, MDL Number 3043.

The deponent is Jennifer Pinto-Martin.

Counsels' appearances will be noted on the stenographic record.

The court reporter is Carrie Campbell and will now swear in the witness.

JENNIFER PINTO-MARTIN, Ph.D., MPH, of lawful age, having been first duly sworn to tell the truth, the whole truth and nothing but the truth, deposes and says on behalf of the Plaintiffs, as follows.

/

DIRECT EXAMINATION

QUESTIONS BY MR. SNIDOW:

Q. Good morning, Dr. Pinto-Martin.

A. Good morning.

Q. My name is J.J. Snidow, and I think you understand I represent the plaintiffs in today's case?

A. I do.

(Pinto-Martin Exhibit 600 marked for identification.)

QUESTIONS BY MR. SNIDOW:

Q. Okay. I'm going to show you a document that I've marked as Exhibit 600 of your deposition. We'll be going in that order, from 600 on.

Do you recognize this as your report in this case?

MR. SNIDOW: Do you need those, Jim? Yeah, you do.

THE WITNESS: It does look to be my report with the appendices and the references and my CV, yes.

QUESTIONS BY MR. SNIDOW:

Q. Any changes that you need to make in that report that you've noticed in preparing?

A. So, yeah. In the last week or so I just was reading through it and found a few things that I would like to change.

THE WITNESS: Do I give him this?

MR. MURDICA: They already have it.

QUESTIONS BY MR. SNIDOW:

Q. Is it that handwritten note that you produced?

A. Yes. Yeah. Yeah.

Q. Anything else?

A. No.

Q. So other than those marks that you made on the handwritten note, everything else in your report you believe is accurate as you sit here today?

A. I do.

Q. I'd like you to turn to page 5 of Exhibit 600, which is your report.

A. Uh-huh.

Q. And do you see a paragraph that's marked 7 there?

A. Yes.

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Q. Do you see the sentence that begins "because"?
A. Uh-huh.
Q. It says, "Because the better designed studies do not report an association, the inconsistency in the studies is an important factor that weighs against a causal conclusion."
Did I read that correctly?
A. You did.
Q. Does that sentence apply both to the ADHD and the ASD literature?
A. I believe so.
Q. Okay. And that was important to you as you say here?
A. Uh-huh.
Q. So it was important to you that the better-designed studies don't report an association either for ASD or ADHD?
MR. MURDICA: Objection to form.
Go ahead.
THE WITNESS: Correct.
QUESTIONS BY MR. SNIDOW:
Q. Correct, all right.

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All right. Marking another document as Exhibit 601. This is just my handwriting, and I'll give it to you when we're done in a second.
So tell me what the better-designed studies on ASD are. What are their names?
MR. MURDICA: J.J., I object to the use of this kind of thing. I don't think you can mark it as an exhibit. We're not going to create plaintiff lawyer-created exhibits here.
MR. SNIDOW: Jim, objection to form.
MR. MURDICA: No -- well, hang on. This is different. This is about whether you can create something as an exhibit, and I'm not going to let that happen.
MR. SNIDOW: Okay. I'll take the marker off if that's what you want.
MR. MURDICA: You're not going to be able to mark this as an exhibit

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at the deposition, period, unless you want to call the Court.
MR. SNIDOW: Okay. That's fine. I'm going to use this though.
MR. MURDICA: Okay. Take the marker off. We're not going to mark it, and I'm letting the court reporter know that we won't be marking it as an exhibit.
If you intend to, let's just call the Court now because it's not happening.
MR. SNIDOW: Okay.
QUESTIONS BY MR. SNIDOW:
Q. Dr. Pinto-Martin, do you see this document?
A. I do.
Q. All right. Can you tell me what are the better-designed studies for ASD? What are their names?
MR. MURDICA: J.J., are you going to take that marker off?
MR. SNIDOW: I'm going to, I promise.
MR. MURDICA: Okay.

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MR. SNIDOW: Trust me. I promise.
MR. MURDICA: Okay.
QUESTIONS BY MR. SNIDOW:
Q. Dr. Pinto-Martin, what are the names of the better-designed studies for ASD?
MR. MURDICA: Object to form.
If you can answer it, go ahead.
THE WITNESS: So the best-designed study that uses ASD as a diagnostic outcome of the five that I include in my report that look at prenatal acetaminophen exposure and ASD in the child is the Danish National Birth Cohort study, the Liew 2016 C study.
QUESTIONS BY MR. SNIDOW:
Q. Okay.
A. And I can go into the reasons --
Q. Nope. Nope.
A. -- why I think the others are not as well-designed, if you like, but...
Q. Yeah.
Is Liew 2016 the only study

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that you're referring to in your report when you are referring to the better-designed studies?
A. With respect to ASD, yes.
Q. All right. So just Liew 2016?
A. Yes.
Q. For ADHD, when you referred to the better-designed studies, which studies did you mean?
MR. MURDICA: Object to the form.
THE WITNESS: So the best-designed study that looks at maternal acetaminophen exposure during pregnancy and ADHD as a diagnostic outcome is the Gustavson 2021 study, which is based on the mother and baby cohort from Norway.
QUESTIONS BY MR. SNIDOW:
Q. Okay. Any other better-designed studies that you're referring to there for ADHD?
A. That's the best.
MR. MURDICA: Objection to form.

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You can answer.
QUESTIONS BY MR. SNIDOW:
Q. So just one for each?
A. (Witness nods head.)
Q. So you used the plural there, but there's just one for each of them?
MR. MURDICA: Objection to form.
THE WITNESS: There's one for each them.
QUESTIONS BY MR. SNIDOW:
Q. Okay. And --
A. Two studies in total.
Q. Yeah. And, Dr. Pinto-Martin, you mentioned Liew 2016. It's your testimony that Liew 2016 does not report an association between acetaminophen and ASD?
MR. MURDICA: Objection to form.
THE WITNESS: Liew 2016 has a series of outcome measures that they use that include ASD alone, infantile autism, ASD with hyperkinetic disorder, and the positive association was found for a subset of those

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outcomes, so...
QUESTIONS BY MR. SNIDOW:
Q. Okay. So let's look at your report again. You said, "The better-designed studies do not report an association."
Right?
MR. MURDICA: Objection to form.
QUESTIONS BY MR. SNIDOW:
Q. I asked you, which better-designed studies. You said Liew 2016, right?
MR. MURDICA: Objection to form.
THE WITNESS: Uh-huh.
QUESTIONS BY MR. SNIDOW:
Q. And my question for you is very simple, does Liew 2016 report an association between acetaminophen use and ASD?
MR. MURDICA: Objection to form.
QUESTIONS BY MR. SNIDOW:
Q. Yes or no.
MR. MURDICA: Asked and answered.

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QUESTIONS BY MR. SNIDOW:
Q. Does it do that?
A. It does.
Q. Okay. So I'm going to cross this one off because it does.
What better-designed --
A. So --
MR. MURDICA: Objection to form. Hang on. First of all, I have to object. I object to form. There's no need to raise your voice.
MR. SNIDOW: Okay.
MR. MURDICA: Okay? We can stay calm and professional all day long.
MR. SNIDOW: Yeah, that's fine.
MR. MURDICA: Let's try it.
THE WITNESS: May I --
QUESTIONS BY MR. SNIDOW:
Q. Hold on. Hold on. Hold on. Let me ask the question.
The question is, besides Liew 2016, are there any better-designed studies on ASD that you know of that do not report an association between acetaminophen

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use and ADHD?
MR. MURDICA: Objection to form.
THE WITNESS: The current literature does not include any better-designed studies.
QUESTIONS BY MR. SNIDOW:
Q. Okay.
A. Better-designed is -- we could talk about what that means.
Q. Okay. For Gustavson 2021, is it your testimony that Gustavson 2021 does not report an association between prenatal acetaminophen use and ADHD?
A. It is.
Q. Okay. In that entire study?
MR. MURDICA: Wait. Objection to form.
You can answer.
THE WITNESS: The authors report the previously reported association from the same cohort and the same set of authors and then apply a sibling-control analysis that reduces the prior reported association

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to the null.
QUESTIONS BY MR. SNIDOW:
Q. Okay. But if I just -- if I open up Gustavson 2021, and we will, am I going to find an association between acetaminophen and ADHD in there?
A. At the end of the day, the association that was reported was confounded by genetics, and the final outcome there is a null finding.
Q. Okay. Do you remember my question, though?
A. I do.
Q. Okay. If I open Gustavson 2021, am I going to find an association between prenatal acetaminophen use and ADHD?
MR. MURDICA: Objection to form.
She already answered it.
THE WITNESS: Go ahead?
MR. MURDICA: If you want to do it again, go ahead.
MR. SNIDOW: Hey, Jim, "objection to form." You know we did

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this last time.
MR. MURDICA: Don't ask the same question twice in a row.
MR. SNIDOW: Okay. Let's go off the record.
VIDEOGRAPHER: The time is 8:51 a.m. We're off the record.
(Off the record at 8:51 a.m.)
VIDEOGRAPHER: The time is 8:53 a.m., and we're on the record.
QUESTIONS BY MR. SNIDOW:
Q. Okay. Dr. Pinto-Martin, do you remember the question I asked you?
A. I don't. I'm sorry.
Q. Okay. If I look in Gustavson 2021, am I going to find an association between prenatal APAP use and ADHD, yes or no?
MR. MURDICA: Objection to form.
THE WITNESS: Gustavson 2021 will summarize the results from the whole cohort, and in that entire cohort, as was reported in the prior study by Ystrom and Gustavson and

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others, there was an elevated risk.
He will then go on to apply a sibling-control analysis, which is a technique to control for genetic confounding, a very important confounder in this literature, and will report that that prior result is reduced to the null.
QUESTIONS BY MR. SNIDOW:
Q. Okay. So it's a "yes" --
MR. MURDICA: Object- --
QUESTIONS BY MR. SNIDOW:
Q. -- there's going to be an association reported in Gustavson 2021?
MR. MURDICA: Objection to form.
THE WITNESS: I would say it's a yes and a no. It's a yes, and then it goes on to refute that finding.
QUESTIONS BY MR. SNIDOW:
Q. That's fine. And we'll talk about this the sibling control.
Okay. Dr. Pinto-Martin, this is not your first deposition, right?
A. That's correct.

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Q. And it looks like you've testified on behalf of Pfizer and Ely Lilly related to SSRIs?
A. I've never test -- well, do you call a deposition a test --
Q. I do.
A. Okay. So, yes, I have.
Q. Okay. The Nexium litigation, gave a dep? It's a PPI.
A. Yes.
Q. Okay. I believe you testified in a case about twins with autism who were exposed to tocolytic agents?
A. That's correct.
Q. And then a case where parents were occupationally opposed {sic} to a pesticide; is that right?
A. Occupationally exposed, yes.
Q. Is that it?
A. In terms of deposition, I believe so. I -- you know, it's -- I've been doing it for more than ten years, but I believe you've captured all the depositions I've done, yes.
Q. How about trial testimony?

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A. I've gone to court once. That was in the twin case that you described where they were exposed to a tocolytic, which is an agent to prevent preterm labor.
And we went to a court in Maryland, and it was in front of a judge, I believe it's what's called a Daubert hearing. There was not a jury there, but I was examined, cross-examined, in front of the judge.
Q. Okay.
A. That's my only court appearance.
Q. All right. So as far as you can remember four -- sorry, five: Four depositions and one trial testimony?
A. That's sounds about right, yeah.
Q. Have you ever testified on behalf of a plaintiff?
A. I've never been deposed. I have been engaged on behalf of plaintiffs and done consultation, but I've -- that -- those consultations have never proceeded to a deposition.

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Q. What cases were those?
A. I would have to go back and look at my records to remember the specifics.
Q. Okay.
A. And I believe that they're protected, so I don't know that I can disclose the specifics of the -- of the cases.
Q. All right. But for testimony, depositions or trial, it's been only on behalf of defendants?
MR. MURDICA: Objection to form.
THE WITNESS: For depositions and the one time I appeared in court, it was -- those were all on behalf of defendants, correct.
QUESTIONS BY MR. SNIDOW:
Q. And in any of those depositions or trial testimony, did you give the opinion that the substance caused whatever the injury was?
A. In the depositions and the trial testimony that I gave, my opinion was that the agent, whatever it was that we were

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considering, was not causally related to autism spectrum disorder, which was the outcome we were looking at.
Q. In the PPI case, you testified that PPIs don't cause fractures?
A. I don't remember the specifics of the PPI case, but I do recall that the -- that the opinion that I gave was not in -- did not implicate the agent.
Q. Do you know whether that label now warns about bone fractures?
MR. MURDICA: Objection to form.
THE WITNESS: I do not.
QUESTIONS BY MR. SNIDOW:
Q. Okay. Have you done any consulting for pharmaceutical companies?
A. I have not.
Q. Do you sit on any boards, advisory boards, anything like that, of pharmaceutical companies?
A. I do not.
Q. Any other work for pharma companies I've forgotten?
A. No.

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Q. Have they ever sponsored your research?
A. They have not.
Q. Have you ever done any media training?
A. I have not.
Q. Do you know anyone who works at Johnson & Johnson?
A. Not to my knowledge.
Q. Do you know -- before this litigation, did you know any of the other experts involved in this case on either side?
A. I had certainly heard of some of them. I don't know any of them personally.
Q. Never met them at academic conferences?
A. No.
Q. And that's true both for the defense experts and the plaintiff experts?
A. Correct.
Q. So what, that's ten or so?
A. I think so, yeah.
Q. And never met any of them in your work as an epidemiologist?

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A. No.
Q. Your billing rate is $750 per hour?
A. That's correct.
Q. And if I'm reading your time entries right, you've spent more than 200 hours on this case so far?
A. That's correct.
Q. So more than $150,000 so far?
A. That's correct.
Q. Does that money go to you or to Penn?
A. That money goes to me.
Q. Do they know you're doing this work?
A. I do not have to disclose this work by the rules of Penn.
Q. Sorry. So that's a "no," they do not --
A. They do not know.
Q. And you've reviewed the Penn HR policies before deciding not to disclose to them that you're doing this work?
A. Of course I have.
Q. And you're aware there's a

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policy that all extramural and intramural activities should be cleared through the individual's immediate supervisor when these activities constitute a possible conflict of interest; is that right?
A. I do sign a conflict of interest statement. I have no conflict of interest, and so there's nothing to report.
Q. You're an autism researcher professionally, right?
A. I'm a professor professionally.
Q. Well, but you focus on autism research?
A. I do.
Q. I didn't think you were going to fight me on that.
And it's your testimony that giving testimony on behalf of J&J about what does and doesn't cause autism doesn't constitute a conflict of interest?
MR. MURDICA: Objection to form.
THE WITNESS: I'm not giving testimony on behalf of anyone. I'm giving testimony based on my expert

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review of the epidemiologic literature. That's what I was asked to do, and that's what I've done.
QUESTIONS BY MR. SNIDOW:
Q. You spent a significant part of your career working to identify modifiable risk factors for ASD; is that right?
A. I continue to work on that.
Q. What's a modifiable risk factor?
A. Modifiable risk factor is something that we -- is a risk factor we can do something about. So it's a risk factor that we can intervene on and thereby reduce the risk of an outcome.
Q. And I think I know, but just to clarify. When you're using "risk factor," at least in the way you just did, you're referring to something that's actually causal, right?
A. I'm glad you asked that question.
Q. Yeah.
A. And the answer is no. So we have risk factors in epidemiology that get

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evaluated with respect to their impact on an outcome. So a risk factor can be null; in other words, there is no association. It can be -- it can show evidence of an association, which then puts it in the category of potentially causal, but it's not -- a risk factor does not equate with a causal agent.

Q. Well, how about modifiable risk factor?

MR. MURDICA: Objection to form.

QUESTIONS BY MR. SNIDOW:

Q. I mean, if you're going to modify it and expect a lower risk, it seems like it's got to be causal, right?

MR. MURDICA: Objection to form.

You can answer.

THE WITNESS: So there's association and there's causality. And in observational epidemiology, which is what we're talking about here, we are establishing an association. We are looking at the body of evidence to see if the --

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there is a credible association between the factor that we're studying and the outcome that we're studying.

We cannot establish causality in an observational study because it is not an experiment.

QUESTIONS BY MR. SNIDOW:

Q. So it's your testimony you can't ever establish causality without doing an RCT?

A. That's not what I said.

Q. Okay. Well, you said "without doing an experiment."

MR. MURDICA: Objection to form.

There's no question.

QUESTIONS BY MR. SNIDOW:

Q. Well, let me ask it again.

What did you mean when you said we can't ever establish causality with an observational study because it's not an experiment?

MR. MURDICA: Objection to form.

Answer it, if you can.

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THE WITNESS: So observational studies are fraught with methodologic challenges, as I'm sure you are aware, and those challenges render any kind of conclusive results about causality challenging.

There are instances where a set of observational studies are powerful enough to overcome those challenges, and we are able to say they're -- that the evidence supports a causal association.

But that's rare.

QUESTIONS BY MR. SNIDOW:

Q. Right.

Can you give me an example of a modifiable risk factor for anything that's not causal?

MR. MURDICA: Objection to form.

THE WITNESS: An example of a modifiable risk factor?

So --

QUESTIONS BY MR. SNIDOW:

Q. Well, let me ask -- let me try

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some examples first.

What's a modifiable risk factor for lung cancer?

A. Smoking would be a modifiable risk factor for lung cancer.

Q. That one's definitely causal, right?

A. I believe that we have strong enough evidence to support there's a causal association between smoking and lung cancer, yes.

Q. All right. That's good.

Can you think of another modifiable risk factor off the top of your head?

A. For lung cancer?

Q. Sure.

A. So I could imagine that air pollution, you know, you know, cities that have high levels of particulate matter, may have higher rates of lung cancer.

The data to determine whether that's causal is going to be very, very challenging because it's an ecological measure. We don't have individual-level

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exposure, so I would describe that as modifiable risk factor for which causal data is not established.
Q. Okay. You're a member of the American College of Epidemiology?
A. Uh-huh.
Q. That's a pretty well-respected organization?
MR. MURDICA: Objection to form.
THE WITNESS: It is.
QUESTIONS BY MR. SNIDOW:
Q. How about the Society For Pediatric Epidemiologic Research?
A. I am a member and -- yes.
Q. And you used to be president.
A. I used to be president.
Q. And that was in '93, '94?
A. Sounds about right.
Q. Is that a pretty good organization?
A. I think it's a reputable organization, yes.
Q. Promotes good science, in your experience?

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MR. MURDICA: Objection to form.
THE WITNESS: In my experience, yes.
QUESTIONS BY MR. SNIDOW:
Q. Doesn't promote bad science in your experience, does it?
A. That's not been my experience.
Q. Okay. You're familiar with the National Academy of Medicine?
A. I am.
Q. Fair to say it's pretty hard to get elected to that?
A. I would agree.
Q. Extremely impressive credential?
A. It's a hard appointment to get, yes.
Q. It's been described as the country's most esteemed and authoritative advisor on issues of health and medicine, right?
MR. MURDICA: Objection to form.
THE WITNESS: I don't know

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where that comes from. I don't know who says that.
QUESTIONS BY MR. SNIDOW:
Q. Are you a member of the National Academy of Medicine?
A. I am not.
Q. Are you familiar with the International Society of Environmental Epidemiology?
A. I've heard of it.
Q. A pretty good organization?
A. I really know nothing about it. It's just that I've heard that name.
Q. How about the Mailman School of Public Health?
A. I certainly know the Mailman School of Public Health, yes.
Q. Is that at Columbia?
A. It is.
Q. Outstanding public health school?
MR. MURDICA: Objection to form.
THE WITNESS: It is.

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QUESTIONS BY MR. SNIDOW:
Q. Do you know anyone there?
A. I do. I did my postdoc at Columbia, so I do know people there.
Q. Who do you know who?
A. I know Ezra Susser who was the chair of epidemiology for many years. I know his father, Mervyn Susser, with whom I worked, and his mother is Zena Stein, with whom I worked.
I did my postdoc with a physician named Nigel Paneth, who is no longer there. Various other folks. I was there for four or five years, so...
Q. And Irwin {sic} Susser, outstanding epidemiologist?
A. So Mervyn Susser is no longer alive. That's the father.
Q. But he was.
A. He was -- he was a very, very good epidemiologist, yes.
Q. And he was chair of the epidemiology department at Columbia?
A. No, I'm sorry. I think you're getting them confused.

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So Ezra Susser was his son, and Ezra was the chair.

Q. And was he a pretty good epidemiologist?

MR. MURDICA: Objection to form.

THE WITNESS: Ezra has a very good reputation.

QUESTIONS BY MR. SNIDOW:

Q. Okay. How big does a risk ratio need to be before you would say it was strong?

MR. MURDICA: Objection to form.

THE WITNESS: So that's a difficult question to answer simply because it so depends on the exposure that you're looking at, the outcome that you're looking at, the quality of the data that underlies that exposure, but what we do know is that the stronger a measure of association is the less likely it is to be due purely to confounding or bias.

So I would say, you know,

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there's not a precise number there. I'm not willing to give you a precise number because it depends so much on the context.

QUESTIONS BY MR. SNIDOW:

Q. That's what I was asking.

It's not 2.0, 3.0. You can't do it like that?

A. That's not how I do it.

Q. You think it would be wrong to just set a cutoff, right? Because you have to consider all of the data, right?

MR. MURDICA: Objection to form.

THE WITNESS: I think different epidemiologists and biostatisticians approach the question differently. The way I approach it is that there's not a right number that you need to exceed.

QUESTIONS BY MR. SNIDOW:

Q. Okay. How many statistically significant results do you need before you think there's an association that's been demonstrated?

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MR. MURDICA: Objection to form.

THE WITNESS: Again --

MR. MURDICA: Go ahead and answer.

THE WITNESS: Sorry. I think I answer too quickly.

Again, that's an impossible question to answer in that sort of theoretical framework. It is very dependent upon the literature that you're reviewing, the specifics of the studies. Statistically significant results can be due to all kinds of bias and confounding, obviously, and they can also relate to a whole range of outcomes, which is important to consider when you're looking at the number of statistically significant associations.

So I can't answer that question.

QUESTIONS BY MR. SNIDOW:

Q. So I think maybe you misunderstood. I'm not asking about

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causation.

I'm just saying, how many results before you would say there's an association? Maybe it's confounding, maybe it's bias, but I think there's an association.

A. Again, I can't give you a number. It's dependent upon the underlying data.

Q. So if I had 500 studies showing a statistically significant link between an exposure and an outcome, you'd say, "I don't know if there's an association"?

MR. MURDICA: Objection to form.

THE WITNESS: Again --

MR. MURDICA: Go ahead.

THE WITNESS: I can't answer that in this theoretical context. I would want to look at the studies. I would understand -- I want to understand how the data was derived. You could have 500 statistically significant studies that were wrong because they were all confounded.

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QUESTIONS BY MR. SNIDOW:
Q. I agree. That's not what I'm asking. So put aside confounding.
Can you do that for me?
MR. MURDICA: Objection to form.
QUESTIONS BY MR. SNIDOW:
Q. Can you put aside confounding?
MR. MURDICA: Objection to form.
Answer the --
THE WITNESS: I will -- I will ignore the idea of confounding to answer your question.
QUESTIONS BY MR. SNIDOW:
Q. And bias, okay, ignore that.
All I'm asking is, for an association, if I had 500 studies showing a statistically significant link, that would be an association, right?
It doesn't mean it's causal, but that would be an association, right?
MR. MURDICA: Objection to form.
THE WITNESS: So you've asked

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me to ignore two things that are absolutely central to observational studies. So you're asking me something that's theoretically impossible. There's no such thing as an observational study that is free of bias and confounding, so I can't answer the question.
QUESTIONS BY MR. SNIDOW:
Q. Okay. How do you define a causal agent?
MR. MURDICA: Objection to form.
THE WITNESS: A causal agent is something for which there is consistent, reliable, valid evidence that the dose of that agent, if you will, increases the risk of the outcome that you're studying.
QUESTIONS BY MR. SNIDOW:
Q. You know what a forest plot is, right?
A. I do.
Q. All right. I'm going to do one as an example. I would mark it, but, you

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know.
All right. So I made up these numbers. But can you tell me on this forest plot what study 1 is showing?
MR. MURDICA: I object to the use of this, but you can answer it, if you can.
THE WITNESS: It says a 1.5 something. I don't know. There's no --
QUESTIONS BY MR. SNIDOW:
Q. And that is a relative risk.
A. Okay. So you're telling me those top numbers are relative risk?
Q. Yes.
A. So it shows you that there's a 1 point -- something like 1.5, 1.6 relative risk with a confidence interval that goes from something like 1.25 to 1 point -- to almost 2.0.
Q. Okay. Is that result statistically significant?
A. This -- I have no idea what this -- what this means in statistical terms. If you had this in a textbook, it would show

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that this is evidence of a statistically significant effect, but it's completely without context here, so...
Q. I know. I'm just -- I promise, I made these up. I'm truly just trying to talk about concepts.
For study 2, essentially same thing, except the point estimate is somewhere around 2.3; is that right?
A. That looks about right.
Q. Right.
And it is statistically significant, right?
A. Again, the confidence intervals do not include 1.
Q. Study 3, the point estimate looks like maybe 1.2?
A. Maybe 1.1.
Q. Yeah, maybe 1.1.
And that one is not statistically significant, right?
A. Confidence intervals include 1, which would indicate that you cannot rule out chance as an explanation for that --
Q. Okay.

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A. -- whatever it is.
Q. Yeah.
All right. And then the last one there, study 8, similar point estimate, but the confidence intervals are wider, right?
A. Correct.
Q. Okay. And it's not statistically significant, right?
A. Confidence intervals include 1.
Q. Would you -- would you characterize this as a strong association?
MR. MURDICA: Objection to form.
THE WITNESS: I cannot answer that question.
QUESTIONS BY MR. SNIDOW:
Q. Okay.
A. Because without the context of the underlying data, I have no way of judging whether it's strong or not.
Q. How about a consistent association? Would you say this is consistent?
A. I would say the same thing for

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consistency. Without understanding how these results were derived --
Q. Yeah.
A. -- I cannot determine whether there's consistency.
Q. The only reason I ask is because in your report, if I read it correctly, you suggest that the presence of statistically nonsignificant findings means that the results can't be consistent; is that right?
MR. MURDICA: Objection to form.
THE WITNESS: In my report, I state that statistical significance is relevant to my consideration for consistency. It is not the only criterion by which I judge consistency.
But I certainly take that into account when I'm looking to see whether a body of literature has consistent results.
QUESTIONS BY MR. SNIDOW:
Q. Let me ask it a different way.

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Can a set of results ever be consistent if some of the confidence intervals overlap with 1?
MR. MURDICA: Objection to form.
THE WITNESS: It depends on your definition of consistency. The way I derive consistency, it includes an evaluation of the statistical significance of the results and a whole host of other things, which I'm happy to talk to you about.
QUESTIONS BY MR. SNIDOW:
Q. But can you answer my question? Can a set of results ever be statistically significant if -- sorry, strike it.
Can a set of results ever be consistent if some of the results are not statistically significant?
MR. MURDICA: Same objection.
THE WITNESS: I cannot answer that question in a theoretical context like that. I would need to know exactly what you're talking about. I would need to understand the

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underlying data. I can't do it --
QUESTIONS BY MR. SNIDOW:
Q. Okay.
A. -- in isolation.
Q. All right. But on this one, I want to talk about this result, study 7.
This is showing a point estimate below 1?
A. Correct.
Q. What's that indicate?
A. Well, in most cases, depending on what these data mean, that is a protective effect of the exposure on the outcome.
Q. And that one is statistically significant as well, right?
A. It shows a statistically significant protective effect for whatever it is. Again, without any knowledge of the underlying data, that's, you know, hard to say.
Q. Okay. All right. You know what a prospective cohort study is?
A. I do.
Q. And so the way those work is you identify a group of unexposed and exposed

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groups, right?
A. Typically that's the way you enroll individuals into a prospective cohort study.
Q. And then you follow them over time to see which ones develop the outcome of interest?
A. That's right.
Q. And if the same percentage develop the outcome of interest, that's equivalent to a risk ratio of 1.0?
MR. MURDICA: Note my objection to the use of the demonstrative.
MR. SNIDOW: Got it. Got it.
MR. MURDICA: And object to the form of the question.
QUESTIONS BY MR. SNIDOW:
Q. If the same percentage develop the outcome, it's equivalent to a risk of 1.0?
A. Again, you know, this is -- these are such sort of theoretical concepts.
Q. Okay.
A. But, yes, theoretically, that's the way it works.

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Q. Okay. And so if you see something like this, that doesn't give you a signal one way or another, does it?
MR. MURDICA: Objection to form.
THE WITNESS: I would say that's a null finding.
QUESTIONS BY MR. SNIDOW:
Q. Right.
Exactly a null finding. It's 1.0 on the dot.
A. Perfect.
Q. Yeah, perfect.
A. A perfect finding.
Q. And even if there are, you know, tiny differences between the groups like this, still probably a null finding. You'd have to do the math, but probably a null finding, right?
MR. MURDICA: Objection to form.
THE WITNESS: Again, really hard to say just based on a chart like this, but I don't see a big difference between those two groups.

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QUESTIONS BY MR. SNIDOW:
Q. Right.
There's only one more person that got the outcome of interest in the exposed, right?
A. Right.
Q. All right. So null finding again.
So but you would agree if -- I did 100 kids here, but if these actually represented a million kids in each arm, that could still be a statistically significant result, right?
MR. MURDICA: Objection to form.
THE WITNESS: I would want to do the numbers and understand what we were talking about in terms of exposure. I would want to know how that exposure was ascertained. I would want to know the reliability and the validity of that exposure.
I cannot answer a question, you know, like whether it would be significant or important without the

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context.
QUESTIONS BY MR. SNIDOW:
Q. Well, you can for the statistical significance, right? You can just run the math.
MR. MURDICA: Objection to form.
THE WITNESS: Again, statistical significance depends on the quality of the data underlying it. You can have a statistically significant result that is flawed because the underlying data is biased.
QUESTIONS BY MR. SNIDOW:
Q. I totally agree. And that's why I say, please set that aside. I'm just saying --
A. It's very hard to do.
Q. No, I know, but for the numbers it's not, right?
You could run the math and see whether these are statistically significant differences, right?
MR. MURDICA: Object to form.

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QUESTIONS BY MR. SNIDOW:
Q. Is that right?
MR. MURDICA: Note my objection.
MR. SNIDOW: Yeah. I got -- I got the objection --
MR. MURDICA: I can't --
MR. SNIDOW: Ah-ah-ah, you promised. You promised.
MR. MURDICA: I can't sit here forever with you asking the same question with the -- with this made-up thing.
MR. SNIDOW: Jim? Jim, we talked in the hallway. You promised.
MR. MURDICA: Okay. But you still have to conduct yourself in accordance with the rules.
MR. SNIDOW: Okay.
QUESTIONS BY MR. SNIDOW:
Q. Ma'am, is that right, you can run the math and determine whether or not these are statistically significant?
A. I would say you could run a mathematical equation to determine the

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relative risk in this, you know, artificial example, but it's meaningless in my mind without the underlying context.
Q. Sure.
This is equivalent to a relative risk of 1.5?
MR. MURDICA: Objection to form.
THE WITNESS: Do you want me to count them?
QUESTIONS BY MR. SNIDOW:
Q. Yeah. I promise, it's -- it's 25 in the exposed and 20 in the unexposed. Oh, sorry. It's 30 in the exposed and 20 in the unexposed.
A. I'm sorry, so what's the question?
Q. Risk ratio is 1.5.
MR. MURDICA: Objection to form.
QUESTIONS BY MR. SNIDOW:
Q. Is that right?
A. Are you asking me or telling me? You just told me.
Q. I'm --

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A. Are you asking me whether I agree with you?
Q. I'm asking, yeah. Is that right?
A. So again, I -- mathematically that is a correct analysis. It is meaningless without the context of the underlying data.
Q. Okay. And this is a risk ratio of 1.2, right -- or sorry, 2.0?
MR. MURDICA: Objection to form.
QUESTIONS BY MR. SNIDOW:
Q. Is that right?
A. Again, mathematically if you were to run these numbers, I believe you would come up with a risk ratio of 2.0. It is meaningless without the underlying context.
Q. That's a doubling of the risk?
A. 2.0 is equivalent of the doubling of the risk.
Q. Also known as 100 percent increase in the risk, right?
A. That is also referred to as

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100 percent increase in the risk.
Q. And as you said before, as the risk ratio increases, the likelihood of a chance finding goes down?
MR. MURDICA: Objection to form.
THE WITNESS: So in general, that is the way we think about it. The larger the risk, the less likely it is to be explained away by bias and confounding.
It does not mean it's impossible to explain it away by bias and confounding. I think that's very important to consider here.
QUESTIONS BY MR. SNIDOW:
Q. That actually wasn't my question. That was going to be my next one.
My question was, as the risk ratio increases, the likelihood of a chance finding goes down?
MR. MURDICA: Objection to form.
THE WITNESS: So chance is one of the things that we worry about in

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terms of statistical significance, and we can never absolutely determine whether we can rule out chance as an explanation because we have typically one study that we're relying on.

And we're saying, does the evidence from this study overwhelm the possibility that chance explains the finding. We could be wrong.

QUESTIONS BY MR. SNIDOW:

Q. Okay. Do you remember my question, though?

MR. MURDICA: Objection to form.

QUESTIONS BY MR. SNIDOW:

Q. Do you remember it?

A. I thought I answered it. I'm sorry.

Q. My question was, as the risk ratio increases, the likelihood of a chance finding goes down?

I know it's not zero, but the likelihood goes down, right?

MR. MURDICA: Objection to form.

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THE WITNESS: I think that that, again, is very hard to state, you know, a definitive answer to in the absence of context.

QUESTIONS BY MR. SNIDOW:

Q. Okay. All right. If you had a study like this, this doubling of the risk in the exposed group, you would agree and you said, the options are it could be -- it could be chance, right? Is that right?

A. Yeah.

Q. It could be bias?

A. Uh-huh.

Q. And do some epidemiologists say that confounding's a type of bias?

A. That's fine. I can -- I can accept that.

Q. But I'll say it, it can be confounding?

A. It can be confounding.

Q. And the remaining option is causation, right?

MR. MURDICA: Objection to form.

THE WITNESS: If you rule out

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all of the others, then you have evidence in support of a causal association.

I wouldn't say you've established causation. I think there's a difference in the way I phrased that that's an important one.

QUESTIONS BY MR. SNIDOW:

Q. Helpful.

My question, though, is, are there other theoretical possibilities for what's going on here besides chance, bias, confounding and causation?

MR. MURDICA: Objection to the form and the continued use of this hypothetical demonstrative.

THE WITNESS: In standard epidemiologic textbook explanation, no.

QUESTIONS BY MR. SNIDOW:

Q. All right. That's where I got it from, so thank you.

Oh, and actually, I'll just say it. This is basically how the link between tobacco and lung cancer was detected, right?

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They noticed that people exposed to tobacco had much higher risks of lung cancer?

MR. MURDICA: Objection to form.

THE WITNESS: So the history of the association between tobacco and lung cancer goes way back. There are hundreds, possibly thousands, of studies that involve all different kinds of study design. A prospective cohort study would certainly be one of those.

There are case-control studies. There are ecological studies. There are all kinds of pieces of evidence that support the notion of a causal link.

QUESTIONS BY MR. SNIDOW:

Q. Right.

But -- I totally agree. But I'm just asking, they originally detected the link, originally in the '20s through the '60s, by looking at people who were exposed to tobacco versus people who weren't, right?

A. That's correct.

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Q. And they noticed the people who were had a much higher rate?
A. That's correct.
Q. And then they ruled out bias and confounding and chance, right?
MR. MURDICA: Objection to form.
THE WITNESS: Over time those were ruled out.
QUESTIONS BY MR. SNIDOW:
Q. Over time.
And that's how they made the causal inference, right?
A. I agree.
Q. That's what the Surgeon General did?
A. I agree.
Q. Okay. In your report you state your belief that ASD is primarily caused by genetics; is that right?
A. That's right.
Q. And you think genetics are a primary cause of ADHD as well?
A. I do.
Q. Do you agree that the

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heritability for ASD and ADHD is not 100 percent?
A. I do.
Q. And that means that environmental factors play a role, right?
A. That means that factors other than those that are passed down from the mother and father to the fetus could have an influence. We don't know, but that's possible.
Q. Okay. Including environmental factors?
A. So, yes. Environmental factors I would describe as anything other than genetic factors.
And so that would include lifestyle factors. That would include de novo mutations that are not passed down from the mother and father but that are genetic in origin. And it would include things in the environment.
Q. You agree there are some diseases that are entirely genetic, right?
MR. MURDICA: Objection to form.

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THE WITNESS: Some diseases, certainly.
QUESTIONS BY MR. SNIDOW:
Q. Down syndrome is a good example?
A. Yes.
Q. Identical twins will either both have Down syndrome or neither have Down syndrome, excluding some rare mosaic cases, right?
A. I don't know the genetics of Down syndrome, but that would make sense to me if it's a single gene disorder and they're identical twins that have the same set of genes.
Q. Well, you know it's a replication of the 23rd chromosome?
A. Uh-huh.
Q. And that's something that happens at conception?
A. Uh-huh.
Q. Immediately, right?
MR. MURDICA: Objection to form.
THE WITNESS: Again, I'm not an

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embryologist, but...
QUESTIONS BY MR. SNIDOW:
Q. Okay. Well, you don't -- I mean, do you not know that Down syndrome is -- occurs initially when the egg is fertilized?
A. I do know that.
Q. And that -- that's the monozygotic egg, right?
A. Yes.
Q. So when it splits, they're either both going to have Down's or neither is, right?
A. A single gene disorder, that's how it works.
Q. And autism is not like that, is it?
A. No.
Q. No.
You agree that autism is not caused entirely by genetics, true?
MR. MURDICA: Objection to form.
THE WITNESS: As we said, heritability is not 1 or 100 percent,

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however you prefer to speak of it, so there are other factors.

QUESTIONS BY MR. SNIDOW:

Q. Okay. The reason you know that, in part, is because the concordance for monozygotic twins for autism, it's not 100 percent, is it?

A. Correct.

Q. And what's the -- I know the estimates keep changing.

What do you think the best estimate for that is now?

A. Heritability?

Q. No, for the concordance of monozygotic twins.

A. I would say around 90 percent, but, again, it varies depending on who's doing the study.

Q. So it's -- basically, that estimate has stayed the same for the last ten years or so?

A. It's bounced around a little bit, but yes.

Q. And outside of some rare cases, like Fragile X, you agree there's no single

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gene for autism?

A. There's no single gene for autism, right.

Q. You've never counseled someone to get genetic counseling if they had a child with autism?

MR. MURDICA: Objection to form.

THE WITNESS: So I'm not a geneticist, and I don't counsel patients. So I'm not going to opine on that.

QUESTIONS BY MR. SNIDOW:

Q. Oh, you wouldn't take a position on that?

A. I'm not -- it's not my area of expertise.

Q. So if someone asked you whether you'd counsel someone to get genetic testing, you'd say, "I can't take a position on that"?

MR. MURDICA: Objection to form.

THE WITNESS: I would say I'm not a geneticist, and I don't counsel patients, so I wouldn't try to do

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that.

MR. SNIDOW: Can we play tab NN? And I've still got the ELMO.

Do you want to go off the record, Michael?

MICHAEL KAUFFMANN: Yeah.

MR. SNIDOW: Okay. Go off the record.

VIDEOGRAPHER: The time is 9:28 a.m. We're off the record.

(Off the record at 9:28 a.m.)

VIDEOGRAPHER: The time is 9:32 a.m., and we're on the record.

MR. MURDICA: Okay. I would just like to ask that this is twice now that plaintiff's counsel has unilaterally gone off the record. I asked off the record respectfully that there be consent to do that or at least a discussion in the future.

So this is my notation on the record that that's my request.

Thank you.

MR. SNIDOW: That's fine. All right. Can you play NN?

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(Video played.)

QUESTIONS BY MR. SNIDOW:

Q. All right. Dr. Pinto-Martin, is that you?

A. That is.

Q. All right. And that was in about 2014, I think?

MR. MURDICA: Objection to form.

THE WITNESS: That's probably about right.

QUESTIONS BY MR. SNIDOW:

Q. And she asked you whether you'd counsel someone to get genetic testing, right?

A. I can't remember precisely what her question is, but that's what we were talking about.

Q. Do you want to play it again?

A. No, I mean --

Q. Okay.

A. Yeah.

Q. And you didn't say, "Oh, I can't say anything about that," right? You just said no; is that right?

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MR. MURDICA: Objection to form.
THE WITNESS: I didn't just say no. I described what I think about in terms of the value of genetic testing.
QUESTIONS BY MR. SNIDOW:
Q. In that clip, did you ever say, "Oh, I can't talk about that"?
MR. MURDICA: Objection to form.
THE WITNESS: Again, this was a discussion about the value of genetic testing. I would still -- had she asked me, "Do you individually counsel patients," I would have said no. The situation does not change.
MR. MURDICA: Do you have the entire video? Sorry.
MR. SNIDOW: Yeah.
MR. MURDICA: I don't want to interrupt the question.
MR. SNIDOW: We'll send it to you.
MR. MURDICA: Well, look, if you're going to ask her about the

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whole thing, if you're going to say "you never said this," I think she's got to see the whole thing.
MR. SNIDOW: That's fair. That's fair. That's fair.
MR. MURDICA: So don't ask any more questions like that.
QUESTIONS BY MR. SNIDOW:
Q. Do you agree that you need an environmental trigger in addition to genetics to actually trigger the autism?
A. I don't believe we know the answer to that. So we know that it's highly heritable, and we know that there are some other factors that matter, but those other factors might also be related to genetics.
Q. But you don't -- you wouldn't agree that you need an environmental trigger in addition to genetics?
A. I think that was the thought --
Q. Uh-huh.
A. -- in the past, and I think that I have -- my thinking has evolved since then, and I don't know that we need an environmental, quote/unquote, trigger.

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Q. Okay.
MR. SNIDOW: Let's look at tab LL.
(Video played.)
MR. MURDICA: Okay. Before you ask a question, if this were -- if you were cross-examining via prior sworn testimony, like a deposition transcript, you'd have to show the entire transcript when you were cross-examining.
Instead, you're taking little video clips without the whole context, which I don't think is proper examination, and so I object.
I don't actually think you can do this, J.J.
MR. SNIDOW: Okay. Are you done?
MR. MURDICA: I'm trying to decide if --
MR. SNIDOW: Yeah. We can go off the record and call the judge.
MR. MURDICA: All right. Is this your last one, or do you have a

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lot of these?
MR. SNIDOW: It's on YouTube. Go YouTube it. Okay? Are you done?
MR. MURDICA: But you would need to examine with the entire thing.
MR. SNIDOW: All I'm asking is whether we're calling -- I'm not going to play a 40-minute video in the deposition, obviously. We'll send you the YouTube link if you don't have it, although I suspect you do.
MR. MURDICA: I don't have it.
MR. SNIDOW: Okay. Well, are we going to call the judge, or are we going to go on?
MR. MURDICA: Are you to going ask a question about the entire conversation?
MR. SNIDOW: I'm going to ask her a question.
MR. MURDICA: All right. Let's hear it.
QUESTIONS BY MR. SNIDOW:
Q. My question is, is that you, Dr. Pinto-Martin?

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A. That's still me.
Q. Okay. And I noticed in there that it said that the concordance for twins was 65 or 70.
Is that dated data?
A. So you yourself pointed out this was in about 2014.
Q. Yeah.
A. So, yes, our knowledge has evolved.
Q. That's all I was asking.
It's still not 100 percent, though, right?
A. Correct.
Q. And you did say in there that you need an environmental trigger in addition to the genetics to actually trigger the autism, right?
MR. MURDICA: Object to form.
THE WITNESS: I said that in 2014 based on our best evidence at that time.
QUESTIONS BY MR. SNIDOW:
Q. And since 2014, has the concordance for identical twins gone to

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100 percent?
A. As we have already discussed, it's not 100 percent. It's closer to 90 percent.
Q. Do you agree that there are things that happen to the fetus in utero that predispose a child to autism?
A. I don't think we know the specifics of intrauterine effects on the fetus that might cause autism. We are very interested in studying what those effects might be, but I would say we're still in the early stages of understanding what those factors might be.
Q. Do you think the most important place to look when searching for causes of autism is the gestational period?
MR. MURDICA: Objection to form.
THE WITNESS: I believe that autism is a congenital disorder so that the effect happens in utero. We can't detect it right away, but a child is born with or without autism.

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QUESTIONS BY MR. SNIDOW:
Q. Do you think that the things that happen in utero is where you should look to find causes of autism?
A. I think genetics is where you should look to find causes of autism. I think 90 percent of autism is explainable by heritable factors. That's a huge proportion.
Q. And the other 10 percent?
MR. MURDICA: Objection to form.
THE WITNESS: The other 10 percent we don't know.
QUESTIONS BY MR. SNIDOW:
Q. Okay.
A. And the other 10 percent could, in fact, be tied to genetic factors. So we're, as I said, exploring very intensely to understand what the risk factors are and we don't have the answers yet.
MR. SNIDOW: Let's play tab KK.
(Video played.)
QUESTIONS BY MR. SNIDOW:
Q. You said that, right?
A. I said that.

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Q. And you referred to causal agents in that video, right?
MR. MURDICA: Objection to form.
THE WITNESS: I think I used that terminology, yes.
QUESTIONS BY MR. SNIDOW:
Q. In utero causal agents, right?
A. And this was in 2014.
Q. Do you agree that prenatal environmental exposures can alter the brain?
MR. MURDICA: Objection to form.
THE WITNESS: I'd like you to cite something specific. That's a very general statement. I think there -- there can be evidence, but I would like you to be specific.
(Pinto-Martin Exhibit 602 marked for identification.)
QUESTIONS BY MR. SNIDOW:
Q. Okay. Can I have tab AAA also? Yeah. And also that second book.
All right. You've seen this before?

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A. Uh-huh.
Q. Okay. Did you write a chapter in this book?
A. I was part of a team that wrote a chapter for that book.
Q. Okay. So here's what I'm going to do. I excerpted the entire chapter here.
A. Okay.
MR. SNIDOW: Jim, if you'd like the whole book, be my guest.
MR. MURDICA: Thank you.
MR. SNIDOW: And I'm going to mark this one as 602.
QUESTIONS BY MR. SNIDOW:
Q. All right. And on the first page, that's your name, Jennifer Pinto-Martin?
A. Correct.
Q. And you wrote or co-authored this chapter?
A. I did.
Q. And on 499 at the bottom, do you see where it says "Ongoing research"?
A. At the very bottom, yeah.
Q. It says, "Ongoing research is

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examining the role of hormones, infection, autoimmune response, exogenous toxic exposures, and other potential environmental influences that might alter pre or postnatal brain development alone or by altering gene action."
Is that right?
A. I think my --
Q. It skips over to 501.
A. Yeah, I can't read the top of 501 because it's highlighted and then highlighted again.
MR. MURDICA: It's highlighted and copied and blacked out.
THE WITNESS: Yeah, it's like really dark. I can't -- I mean, I believe you if you say that's what it says, but it would be better to have a clean copy.
MR. MURDICA: I'll give you mine.
THE WITNESS: That's also pretty hard to see, but --
MR. SNIDOW: You can't read that?

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THE WITNESS: It does alter pre or postnatal brain development alone or by altering gene actions, yeah.
QUESTIONS BY MR. SNIDOW:
Q. Okay. And what that's saying is prenatal environmental exposures can alter the brain.
MR. MURDICA: Objection to form.
QUESTIONS BY MR. SNIDOW:
Q. Is that right?
A. As I said, I think that's a hypothesis that we are putting forth in this chapter.
By the way, can you tell me the date of this? I don't remember when we authored this, but it was a while ago.
Q. I don't --
MR. MURDICA: I can.
MR. SNIDOW: Jim took the book.
MR. MURDICA: It looks like 15 years ago.
MR. SNIDOW: Can you just give the date, Jim?
MR. MURDICA: '08.

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MR. SNIDOW: Thank you.
QUESTIONS BY MR. SNIDOW:
Q. All right. You can put that aside.
Do you agree that there are environmental factors that can cause autism?
MR. MURDICA: Object to form.
THE WITNESS: I think we are in a very rich time for investigating the role of nongenetic factors for autism. I don't think we have specific environmental factors with -- describing that broadly, right. So all the things that we talked about already: The lifestyle factors and the actual agents in the environment and the potential other genetic factors.
We don't have strong evidence to support a causal association with any of those environmental factors with perhaps the exception of parental age, which, of course, is linked to genetics in ways that we can talk about, if you want.

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So I think that we are in an exploration phase. We have interesting data. We have data that's continuing to evolve, but there is still a lot of questions.

MR. SNIDOW: Okay. Can you play tab MM?

(Video played.)

QUESTIONS BY MR. SNIDOW:

Q. All right. And that's what -- that's what you've tried to do in your work, right?

A. That's right.

MR. MURDICA: Objection to form.

QUESTIONS BY MR. SNIDOW:

Q. And I'm not asking about conclusively, but do you think that there are any environmental factors where it's more likely than not that it causes autism?

MR. MURDICA: Objection to form.

THE WITNESS: So, again, I'm never going to say that I think an environmental factor causes autism.

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QUESTIONS BY MR. SNIDOW:

Q. Oh, okay.

A. But I could say that, you know, is there evidence in support of a causal association. And as I said with parental age, I think there is strong and consistent evidence from all over the world that the older mother and older father both contribute to an increased risk of autism.

Q. But that's it; nothing else?

MR. MURDICA: Objection to form.

THE WITNESS: I think there is interesting evidence in other areas, but nothing that I think is as strong as the parental age finding.

QUESTIONS BY MR. SNIDOW:

Q. And you wouldn't deem any of the other ones causal?

A. Correct.

Q. Do you agree it's possible that there is currently an epidemic of autism?

MR. MURDICA: Objection to form.

THE WITNESS: So I think to

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answer that question -- first of all, no.

QUESTIONS BY MR. SNIDOW:

Q. Okay.

A. And to answer that question, we need to understand what the definition of an epidemic is.

Q. Right.

A. And I'm happy to go into that, if you'd like.

Q. Well, I think you think an epidemic, you need to know the cause, right?

A. It's --

MR. MURDICA: Objection to form.

THE WITNESS: An epidemic is showing an increase in the actual risk of acquiring the disease, not being labeled with the disease, but an increase in the actual risk of acquiring the disease.

We do not have evidence to show -- that would be the incidence, right? We do not have evidence to show that the incidence of autism

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spectrum disorders is increasing, yes, and information to show that the prevalence is increasing, but those are very different things.

QUESTIONS BY MR. SNIDOW:

Q. Yeah.

But do you think you need to know the cause of a disease to say whether it's an epidemic?

MR. MURDICA: Objection to form.

THE WITNESS: So I think that understanding the incidence of disease requires knowing what's driving the increase in incidences.

So I believe we cannot establish that there's an increased incidence in autism spectrum disorder because we don't know entirely what the causal pathway for autism is.

QUESTIONS BY MR. SNIDOW:

Q. But would you agree we don't currently know whether there's an autism epidemic?

MR. MURDICA: Objection to

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form.
THE WITNESS: I would say I believe, based on the data that I've been involved in collecting and publishing, it -- the epidemic is not a function of an increase in incidence; it's a function of a whole host of factors, including increased awareness, change in diagnostic criteria, early age of diagnosis.
So I do not count that as an epidemic because it's not an increase in the risk of acquiring the disease. It's an increase in the number of individuals who are labeled with the disease.
QUESTIONS BY MR. SNIDOW:
Q. Yeah.
So you don't think there's an epidemic?
A. I do not.
MR. SNIDOW: Can we play tab OO?
(Video played.)

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QUESTIONS BY MR. SNIDOW:
Q. Is that you again?
A. That's me.
MR. MURDICA: Objection to form and to the continued use of these short little video clips from a large video.
MR. SNIDOW: Yeah, that's fine.
QUESTIONS BY MR. SNIDOW:
Q. And there you said we don't know whether there's an epidemic, right?
A. So this was in 2014.
Q. Yeah.
A. And I think that that's what I said in 2014.
Q. Okay. Do you agree heritability does not actually tell you what proportion of a trait is determined by the environment?
A. Heritability does not determine what proportion of the trait is determined by the environment. Yes, I agree with that.
Q. A disease can be heritable and still determined by environmental factors?
A. A disease can be heritable, and

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environmental factors can still influence the phenotype, yes.
Q. So if a her -- we had heritability of -- what do you think autism is, 90 percent?
A. 80 to 90 percent.
Q. 80?
That doesn't mean that autism is 80 percent caused by genetic factors, does it?
MR. MURDICA: Objection to form.
THE WITNESS: Again, we understand autism to be a genetic disorder. We understand heritability to describe the proportion of the phenotype that is explained by genes.
We know that that's not 100 percent. We know that there are other factors as we've -- as we've said already that include lifestyle, environment, other genetic factors.
(Pinto-Martin Exhibit 603 marked for identification.)

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QUESTIONS BY MR. SNIDOW:
Q. All right. I'm going to mark a document as Pinto-Martin 603.
You see at the top there, National Institutes of Health?
A. Barely.
Q. Yeah. Not great printing.
Do you see the bullet at the bottom that says, "Heritability does not indicate"?
A. I do.
Q. It says, "Heritability does not indicate what proportion of a trait is determined by genes and what proportion is determined by environment."
Did I read that correctly?
A. That's what it says.
Q. Do you agree?
A. I think I just said something similar to that.
Q. Okay. It says, "So a heritability of .7 does not mean that a trait is 70 percent caused by genetic factors."
Did I read that correctly?
A. That's what that says.

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Q. Do you agree?
A. I agree with that statement.
Q. So if someone said that 70 to 90 percent of ASD cases are caused by genetics because of the heritability rate that you described, that's inconsistent with this, right?
MR. MURDICA: Objection to form.
THE WITNESS: I don't know where this came from. I don't know what this is used for. So it's a little hard for me to re -- respond sort of off the cuff on statements like this.
QUESTIONS BY MR. SNIDOW:
Q. Well, you told me you agreed with that, right?
A. So I understand that heritability is not deterministic, but I believe that 80 to 90 percent of autism is described --
(Audio interruption.)
MR. MURDICA: All right.

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QUESTIONS BY MR. SNIDOW:
Q. All right. Ma'am, let's focus on this. You said you agreed with the sentence, "A heritability of .7 does not mean that a trait is 70 percent caused by genetic factors," right?
A. Again, this --
Q. Wait, sorry. I'm just saying, do -- are you changing your testimony about whether you agree?
MR. MURDICA: Objection to form.
THE WITNESS: I'm not changing my testimony. I'm trying to contextualize it by saying I don't know where this came from, and I don't know exactly who the audience is. I don't know what it's based on.
So it's hard for me to respond to it.
QUESTIONS BY MR. SNIDOW:
Q. Right.
But you said you agreed with the sentence, right?
MR. MURDICA: Objection to

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form.
THE WITNESS: I can agree with something and still have a --
QUESTIONS BY MR. SNIDOW:
Q. Yeah.
A. -- contextualized response, and that's what I'm saying with that.
Q. All I'm saying is -- what this is saying is the heritability of -- for autism of 80 to 90 percent does not mean that autism is 80 to 90 percent caused by genetic factors, right?
MR. MURDICA: Objection to form.
THE WITNESS: I'm not sure I agree with that.
QUESTIONS BY MR. SNIDOW:
Q. Okay. That's fine.
Do you agree that applying Bradford Hill is more like a clinical judgment than experimental science?
MR. MURDICA: Objection to form.
THE WITNESS: So that's not the way I would describe it because I'm

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not a clinician, so I don't apply clinical judgment. I apply epidemiologic judgment.
I would agree that it's applying epidemiologic judgment to a body of literature.
QUESTIONS BY MR. SNIDOW:
Q. When you're doing Bradford Hill, there's no hard-and-fast rules; it is a matter of judgment, right?
A. I believe that it's a matter of expert judgment, yes.
Q. And when researchers are writing their papers, do you agree they're conservative when assessing causal relationships?
MR. MURDICA: Objection to form.
THE WITNESS: It's a very broad statement. I can't answer.
QUESTIONS BY MR. SNIDOW:
Q. All right. PPP.
All I am asking is when they're -- when they're publishing, they're reluctant to say causation, aren't they?

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MR. MURDICA: Objection to form.
THE WITNESS: I can't say that in general. Some people are very willing to say causation. I myself am I think perhaps more conservative than others.
(Pinto-Martin Exhibit 605 marked for identification.)
QUESTIONS BY MR. SNIDOW:
Q. All right. I'm going to mark a document as Pinto-Martin 605. This is the Reference Manual on Scientific Evidence.
MR. MURDICA: Do you have a copy for me?
MR. SNIDOW: I do. I do.
QUESTIONS BY MR. SNIDOW:
Q. This document, just so you know, is about a thousand pages long, so I've excerpted a couple of chapters.
MR. SNIDOW: Jim, this one is widely available, and I think you're familiar with it, too.
MR. MURDICA: I am.

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QUESTIONS BY MR. SNIDOW:
Q. So this is the Reference Manual on Scientific Evidence.
Do you see that?
A. I see that. I don't really know what that -- how it's used or where it's from or any- --
Q. Yeah.
A. I've never seen it before.
Q. All right.
A. But, yes, that's what it says.
Q. You see it's published by the Federal Judicial Center?
A. I see that on the front page.
Q. And if you could turn to the page that's marked 62.
A. 262? I'm sorry.
Q. I'm sorry.
A. It's marked 62? I don't see that.
Q. 262.
A. Marked 262. I don't have a 262. I have a 253, a 254.
MR. MURDICA: I think he put two parts --

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THE WITNESS: I know, but I still don't have a 262.
MR. MURDICA: Hold on. Hold on. Hold on. Hold on. Hold on. Hold on.
THE WITNESS: It goes from 252 to 500 something -- 255.
QUESTIONS BY MR. SNIDOW:
Q. 599, I'm sorry.
A. 590 -- I don't have 599 either. I have 597.
Q. Look at that one.
MR. MURDICA: I don't have 599 either.
THE WITNESS: You want to share?
Okay. I have page 599. I'm going to get my reading glasses out if you don't mind, because that's pretty small.
QUESTIONS BY MR. SNIDOW:
Q. Please.
A. Okay.
Q. And do you see the sentence that begins -- three lines down that begins

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"generally"?
A. Uh-huh.
Q. It says, "Generally researchers are conservative when it comes to assessing causal relationships, often calling for stronger evidence and more research before conclusion of causation is drawn."
Do you see that?
A. That's what that says.
Q. All right. You can put that one aside for now, but hold on to it.
Do you agree that it's ultimately a value judgment about whether the evidence is strong enough to warrant a causal inference?
MR. MURDICA: Objection to form.
THE WITNESS: So I think I would want you to define a value -- what did you say, a value --
QUESTIONS BY MR. SNIDOW:
Q. A value judgment.
A. -- judgment?
Q. Uh-huh.
A. Because I'm not sure exactly

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what you mean by that. There are -- there are a set of criteria, and I try to apply those criteria with rigor and consistency, and I don't consider that a value judgment.

I think that's an expert opinion judgment.

Q. Okay. Do you think that whether evidence is strong enough to warrant the causal inference is open to reasonable debate?

MR. MURDICA: Objection to form.

THE WITNESS: I think that entirely depends on the evidence, so reasonable debate is -- it happens in science, but I can't in -- sort of out of context say "yes" because sometimes the answer would be "no."

QUESTIONS BY MR. SNIDOW:

Q. Do you think people can disagree with one another in good faith about whether the evidence is strong enough to warrant a causal inference?

MR. MURDICA: Objection. Form.

THE WITNESS: Again, I think it

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depends on the body of evidence.

MR. SNIDOW: Can I have X, please?

(Pinto-Martin Exhibit 606 marked for identification.)

QUESTIONS BY MR. SNIDOW:

Q. All right. Marking a document as Pinto-Martin 606.

A. Put this aside?

MR. MURDICA: Uh-huh.

QUESTIONS BY MR. SNIDOW:

Q. All right. Now --

MR. MURDICA: Can I have my copy, please?

MR. SNIDOW: Yeah.

MR. MURDICA: Thank you.

MR. SNIDOW: Yeah.

QUESTIONS BY MR. SNIDOW:

Q. All right. This is a publication Yudell 2013.

Do you see that at the top there?

A. I do.

Q. And if you look down at the bottom, you'll see your name. It's about

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four lines down in the corresponding author box.

A. I haven't found me, but I believe that I'm in there.

MR. MURDICA: I saw it. Right there.

THE WITNESS: Okay. Yeah. Got it.

QUESTIONS BY MR. SNIDOW:

Q. All right. It's defining you as member -- as a member of the working group in autism risk communication ethics, right?

A. That's correct.

Q. And you served on -- in that working group?

A. I did.

Q. And then it looks like you guys published this paper?

A. Well, I wasn't part of the paper itself, but I'm part of the working group.

Q. Do you think you reviewed it before it went out?

A. I don't recall.

Q. Okay. Let's see if you agree.

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On page 10, at the bottom there, do you see a sentence -- sorry, the bottom of the second full paragraph, there's a sentence that begins "finally"?

A. Uh-huh.

Q. It says, "Finally, the notion of sufficient or appropriate evidential support involves value judgments."

Did I read that correctly?

A. That's what that says.

Q. And that's what this working group that you served on said?

A. Again, I don't know who wrote that particular sentence. It looks like it's citing to two other references, and that may have been their language.

Q. Uh-huh.

A. So I don't know who said that.

Q. Do you agree with it?

A. As I just said, it depends on the definition of value judgment. It's not the way I would describe application of the Bradford Hill criteria, which was your original question.

Q. Well, this isn't about Bradford

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Hill, is it?
A. But that was your original question about the --
Q. No, actually --
A. -- an actual value judgment.
Q. No. I actually said whether the evidence is enough to warrant a causal inference?
MR. MURDICA: Object -- that's not a question.
QUESTIONS BY MR. SNIDOW:
Q. Right?
And so look at it again. It says, "Finally, the notion of sufficient or appropriate evidential support involves value judgments."
Right?
MR. MURDICA: Objection to form.
THE WITNESS: That's what it says.
QUESTIONS BY MR. SNIDOW:
Q. Okay. And if you turn to the next page, page 11, at the top of the first paragraph, the one that begins with the next

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page, there's a sentence that says, "Furthermore"?
A. I see that sentence.
Q. It says, "Furthermore, since judgements of sufficient evidence are value laden, there's no good reason to exclude the voices of the broader autism community when considering them."
Right?
A. That's what that says.
Q. Do you agree?
A. I'm not sure exactly what they mean there.
Q. Okay. So you think that even though your name is on the front, you didn't read this before it went out?
MR. MURDICA: Objection to form.
THE WITNESS: I'm not an author on this paper. We had multiple meetings as a group, and this was a publication that was written without my involvement. So I am not responsible for what's --
(Audio interruption.)

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MR. MURDICA: Do you want to go off the record?
MR. SNIDOW: Yes, please.
VIDEOGRAPHER: The time is 9:59 a.m., and we're off the record.
(Off the record at 9:59 a.m.)
VIDEOGRAPHER: The time is 10:10 a.m., and we're on the record.
QUESTIONS BY MR. SNIDOW:
Q. Okay. Dr. Pinto-Martin, I'm going to go through some associations that have been demonstrated in the autism literature, and what I want you to do is tell me whether you think the most likely explanation is chance, bias, confounding or causation.
Okay?
MR. MURDICA: Object to form.
QUESTIONS BY MR. SNIDOW:
Q. Ready?
A. I understand what you're proposing to do.
Q. Okay.
A. It may be that I'm going to want to look at specific studies to inform

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myself about whether one of those is the most likely explanation. I'm not sure I can do it --
Q. That's fine.
A. -- in a vacuum.
Q. If there's one you aren't sure about, you just let me know.
Okay?
MR. MURDICA: Object to form.
QUESTIONS BY MR. SNIDOW:
Q. All right. Thalidomide?
A. So thalidomide, to my knowledge, there is one study that used data and looked retrospectively at whether thalidomide increased the risk of autism spectrum disorder.
There are many problems with a retrospective design like that. We could talk about the problems inherent in recall bias and -- so I would say that the jury is still out on that one, if you will. One study does not establish or disprove the hypothesis of a causal association.
Q. All right. So you don't think it's -- the most likely explanation is

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causation; is that right?
MR. MURDICA: Object to form.
THE WITNESS: Again, I'm willing to give an opinion when we have one study.
QUESTIONS BY MR. SNIDOW:
Q. All right. You wouldn't say that it's established that thalidomide causes autism?
MR. MURDICA: Objection to form.
THE WITNESS: It's -- I would say there is very significant interesting evidence from one study. I would never make an opinion based on a single study.
I think it's interesting. I think it's compelling. We will never be able to do another study because thalidomide is now off the market.
QUESTIONS BY MR. SNIDOW:
Q. Yeah.
A. And, again, with one study and the inherent problems, I can't establish that something is causal.

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Q. Okay. But what do you think the most likely explanation is? Is it chance, confounding, bias or causation?
MR. MURDICA: Objection to form.
THE WITNESS: I would want to look at the study, look at the sample size, look at the exposure, look at the assessment of outcome.
QUESTIONS BY MR. SNIDOW:
Q. All right. That's fine.
Misoprostol?
A. So that's an abortifacient. And so women who wanted to end their pregnancy took that medication. And then those who didn't lose their baby were then followed and autism was assessed in those babies.
Again, I think that there's interesting evidence to suggest that there may be an association with an increased risk of autism among those women, but it's a very complicated study to assess, given the selection bias going into a study like that, and I would want to review the study -- the

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studies very carefully before I answered a question like the one you're addressing.
Q. All right. Air pollution?
A. So, again, there is some data that suggests that particulate matter in the environment, in the air, is associated with an increased risk. There are many problems with the studies.
I referred to this earlier in the answer to one of your questions because air pollution is an ecological exposure. We don't have individual level of air pollution in a pregnant woman. So I believe that there are very interesting data that are very challenging to interpret with respect to any kind of causal connection.
Q. Mother's psychiatric conditions, do you think that's chance, confounding, bias or causation?
MR. MURDICA: Objection to form.
THE WITNESS: So I think maternal psychiatric condition, because it is linked to genetics, has strong and very consistent evidence

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with respect to both ASD and ADHD.
We don't understand the causal pathway from maternal genetics through psychiatric history of the mother to increased risk of autism in the offspring because we don't know how the genes operate.
So, again, I think the evidence there is very strong and consistent and compelling. If you -- if you wanted me to review that body of literature and give you my best estimate, I'd be happy to do that, but --
QUESTIONS BY MR. SNIDOW:
Q. But sitting here right now, can you tell me that mother's psychiatric conditions causes autism? Can you tell me that?
MR. MURDICA: Objection to form.
THE WITNESS: So, again, as I mentioned before, based on observational studies, I will never say that something causes autism.

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QUESTIONS BY MR. SNIDOW:
Q. Okay.
A. I would say that the strength of the evidence on psychiatric history is substantial, and that it looks to be a risk factor that elevates the outcome of autism in offspring.
Q. Okay. Valproic acid?
A. Again, very interesting data. We know a lot about valproic acid because it's a prescription medication, so we know very specific information about the timing and the dose and the duration of valproic acid with respect to a mother's pregnancy.
We also know the indication for use because it's given for very specific reasons: Seizure disorder, migraine. So the evidence is, again, interesting and compelling and I think strong in many cases, and we are still continuing to evaluate it.
Q. Do you think that the evidence for valproic acid right now is strong enough to say it's most likely causal?
MR. MURDICA: Objection to form.

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THE WITNESS: I would want to review the valproic acid studies. I haven't done that in a while, and I think they are still ongoing. I think people are still producing evidence, but I think that, again, the data is interesting, compelling, worthy of further consideration, could well be confounded by genetics.
There could be other explanations for it, so I'm unwilling to say that anything is causal without a thorough evaluation of that literature.
QUESTIONS BY MR. SNIDOW:
Q. Well, you've got two sections on valproic acid in your report, right?
A. I believe that's true, both in the autism and ADHD section.
Q. And you reviewed the literature before writing those sections, I assume.
A. The literature that existed to date, yeah.
Q. Okay. So can you tell me, does that literature make the most likely

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explanation for the valproic acid association causation?
A. Again, from an observational study, I cannot establish causation. I would say that the evidence on valproic acid is suggestive of an increased risk of autism spectrum disorder among women who took it. That doesn't necessarily establish causality.
Q. I agree.
A. Okay.
Q. But you say in your report you don't think that the evidence for Tylenol is enough to establish causation, right?
MR. MURDICA: Object -- objection to form.
THE WITNESS: That's correct.
QUESTIONS BY MR. SNIDOW:
Q. Okay. And I assume that there's some level of evidence where you would have a different opinion, right?
A. So as I said, the things that I think about when I'm trying to evaluate whether there is evidence in support of a causal association -- not cause, but a causal association -- I look at the information on

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the exposure, what is the precision with respect to timing, dose, duration; what is the precision with respect to assessment of outcome.
And in the acetaminophen literature, we have problems in both of those domains, and so it renders my opinion -- supports my opinion, which is that there is not evidence of a causal association.
Q. Right.
I was asking about valproic acid, right? And does the literature for valproic acid support the statement that the most likely explanation is causation?
Does it or no?
MR. MURDICA: Objection to form.
QUESTIONS BY MR. SNIDOW:
Q. Let me ask it a different way.
If we had had a report saying, "We think valproic acid causes autism," and you were writing a report like yours now, would you write, "I do or I don't think that the evidence for valproic acid supports a causal association"?

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MR. MURDICA: Objection to form.
THE WITNESS: So I tried to answer this question a couple of times.
QUESTIONS BY MR. SNIDOW:
Q. Right.
But can you answer it?
A. I'll try again.
Q. Okay. Would you write that sentence? Would you write, "I think the evidence for valproic acid does support a causal association," or would you write, "I think the evidence for valproic acid does not report a causal association"?
MR. MURDICA: Objection to form.
QUESTIONS BY MR. SNIDOW:
Q. Can you answer that question?
If you can't answer it, we'll move on. But can you answer that?
MR. MURDICA: Objection to form.
THE WITNESS: I believe in my report I agree that the evidence

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supports a causal link. That doesn't mean it establishes it --
QUESTIONS BY MR. SNIDOW:
Q. That's fine.
A. -- but it supports it.
Q. That's all I wanted.
The most likely explanation is causation, it's not just certain.
Is that right?
MR. MURDICA: Object to form.
THE WITNESS: I'll agree with that statement.
QUESTIONS BY MR. SNIDOW:
Q. Okay. And maybe I should have clarified this before, but any of these other risk factors we talked about, would you give the same answer that you did for valproic acid?
Like, would you say thalidomide, misoprostol, air pollution, mother's psychiatric conditions, not definitive, but would you say the most likely explanation is causation?
MR. MURDICA: Object to form.
THE WITNESS: We just went

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through them one at a time, and I think I answered them one at a time. I can't answer them as a group because I differ in the -- with respect to the individual agent, and we talked about it.
QUESTIONS BY MR. SNIDOW:
Q. Right.
But are there any of them where you'd say, "I think causation is the most likely, it's just not definitive"?
A. No.
Q. No. Okay.
Same question for fever: Do you think causation is the most likely, even if not definitive, or do you think not enough evidence?
MR. MURDICA: Objection to form.
THE WITNESS: I think fever is a very interesting finding that we've seen replicated over and over again, and we also have some evidence to suggest that it might be confounded by genetics.

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So, again, you cannot cause -- say that something is causally associated if there's a clear -- a confounder, and that's true across the board.
QUESTIONS BY MR. SNIDOW:
Q. So not enough evidence for fever; is that right?
A. Again, I don't want to be black and white like that. The evidence on fever is very compelling. But if fever is a marker for something else, right, for some underlying immune disorder or some genetic factor in the mother, fever itself is not the causal agent, if you will.
So I have to -- I have to always contextualize like that.
Q. But if I said, "I think fever does cause autism," I read a report, and you were writing your report, and you had to write the sentence, "I think there's enough evidence about fever to say it is causal," or the sentence, "I think there isn't enough evidence to say it's causal," which one of those would you pick?

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MR. MURDICA: Objection to form.
THE WITNESS: So I find it frustrating that you're asking me to come down, you know, on a black -- in a black and white way.
QUESTIONS BY MR. SNIDOW:
Q. You came down on one side in this report, right? You said there's not enough evidence on acetaminophen, didn't you?
MR. MURDICA: Objection to form.
THE WITNESS: I did.
QUESTIONS BY MR. SNIDOW:
Q. Okay. Is there enough evidence for fever?
MR. MURDICA: I need to make my objections.
Object to form.
And you need to ask questions. Not, like, dialogue.
MR. SNIDOW: That's fine.
QUESTIONS BY MR. SNIDOW:
Q. Do you think there's enough evidence for fever or no?

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A. I think the evidence on fever is compelling and interesting, and we don't understand the causal pathway --
Q. Okay.
A. -- that would lead from a fever in the mother to an increased risk of autism in the child. And so we need to keep studying it and keep working on it, which is what we're doing.
Q. Smoking?
A. The evidence on smoking is -- are we talking about any outcome, or can you be specific about --
Q. Autism, ASD. If you had to write the sentence, "I think there's sufficient evidence for smoking," or "I think there's not sufficient evidence for smoking," which one would you write?
MR. MURDICA: Object to form.
THE WITNESS: I would -- similar to some of the prior responses, I would say there is interesting evidence. My review of the literature does not suggest that that's a causal association but that

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there may be confounding, and it may represent some other factor unmeasured.
MR. SNIDOW: All right. Can I play tab RR, Michael?
MICHAEL KAUFFMANN: Yeah.
MR. SNIDOW: Thank you.
(Video played.)
QUESTIONS BY MR. SNIDOW:
Q. Is that your voice on there?
A. That is my voice.
Can you tell me when this was --
Q. I believe that one's either July 2011 or January 2012. Both dates are on there.
A. It was a very long time ago.
Q. Well, right.
But in the interim, the evidence on valproic acid has become stronger, right?
MR. MURDICA: Objection to form.
THE WITNESS: So I just want to point out that the things that you're

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pulling up that reflect my opinions are from many years ago, and my thinking about the etiology of autism spectrum disorder and ADHD and other neurodevelopmental disorders has evolved along with the science. So I think that that's what I believed then, and perhaps my opinion would change over time.
QUESTIONS BY MR. SNIDOW:
Q. Okay. Do you think that SSRIs cause autism?
A. I do not.
Q. All right. So you think not enough evidence on SSRIs, right?
MR. MURDICA: Objection to form.
THE WITNESS: So, actually, there's a lot of evidence on SSRIs.
QUESTIONS BY MR. SNIDOW:
Q. No, no, sorry. Not enough evidence to say causation, right?
A. Again --
MR. MURDICA: Objection.
THE WITNESS: This is -- this

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is the problem that I have here. You're asking me to opine on an exposure which we have since learned, including data from our own research, is confounded by psychiatric history of the mother.

So it is a marker for an increased risk but in and of itself does not cause an increased risk. So I can't just say yes or no.

It has been demonstrated that there's an increased association with SSRI, but that is not a causal association because it was confounded by the underlying maternal psychiatric history.

Once you control for that, the association diminishes to the null.

QUESTIONS BY MR. SNIDOW:

Q. That's what I'm trying to get. For SSRIs you think the most likely explanation is confounding; is that right?

MR. MURDICA: Objection to form.

THE WITNESS: I know it's

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confounding.

QUESTIONS BY MR. SNIDOW:

Q. You know it's confounding. Okay.

For thalidomide, here you present it as an environmental risk factor, right?

MR. MURDICA: Object -- objection to form.

THE WITNESS: In 2011, that's how I presented it.

QUESTIONS BY MR. SNIDOW:

Q. Has there been another study on thalidomide since then?

A. No. And as I said, we will never have another study. We had one study. So in 2011 I was willing to characterize it that way.

Q. Yeah.

A. I think I'm a little more careful now because one study does not establish that something is causal.

Q. I'm sorry. I just want on the record: There hasn't been a thalidomide study between 2011 and now, has there?

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A. Not to my knowledge.

Q. All right.

A. I haven't searched the literature, but I can't imagine how one -- someone would do one.

Q. I couldn't either. That's why I was asking.

Do you think any of the ones we went through - the thalidomide, misoprostol, fever, valproic acid, smoking - do you think there are ones that are -- where there's room for disagreement among epidemiologists about whether they're causal or not?

MR. MURDICA: Objection to the form.

THE WITNESS: So you asked me about a whole host of questions. I think you need to go through them one at a time.

QUESTIONS BY MR. SNIDOW:

Q. Okay. That's fine.

A. And we could really then determine.

Q. Do you think there's room for disagreement on whether thalidomide is

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causal?

A. I think there's room for disagreement on whether someone would characterize it as causal --

Q. Okay.

A. -- based on a single study.

Q. Great.

Misoprostol, do you think there's room for disagreement on whether misoprostol is causal?

MR. MURDICA: Objection to form.

THE WITNESS: Again, it's -- it depends on how you define causal, right, and how you interpret that statement. Personally, I would not be willing to assign causality on the basis of observational studies.

Other epidemiologists may be more willing to do that, so we may have different opinions based on our willingness to assign causality on the basis of observational data.

QUESTIONS BY MR. SNIDOW:

Q. And nothing wrong with that,

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right? It's just disagreements --
A. It's the way it works.
MR. MURDICA: Objection to form.
QUESTIONS BY MR. SNIDOW:
Q. It's the way it works in science generally, right?
MR. MURDICA: Objection to form.
THE WITNESS: It's a broad statement. It's the way it works in my world of epidemiology -- perinatal epidemiology.
QUESTIONS BY MR. SNIDOW:
Q. That's right.
For fever, do you think there's room for disagreement about whether it's causal?
A. So I would say for fever, it's not really about disagreement as much as nuanced understanding of what fever represents and a sense of we need to know more. You know, is it confounded by genetics? Is it -- is it immune dysfunction?
I think fever has interesting

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data that deserves further exploration.
Q. But let me ask it this way. If someone said, I think fever does cause autism, do you think that's a reasonable position or no?
MR. MURDICA: Objection to form.
THE WITNESS: I think it depends on the person and the context in which they're saying that.
QUESTIONS BY MR. SNIDOW:
Q. If an epidemiologist, one of your colleagues, came to you and said, hey, I actually think fever is causal, I know you disagree, do you think that's a reasonable thing for them to say or not?
A. I think it's perhaps a naïve thing because it's a not a very nuanced understanding of how fever might relate to an increased risk of autism.
Q. Okay.
A. Is it wrong? It depends on how you define "causal."
Q. For ADHD, besides genetics, are there any risk factors that you think there

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is enough evidence to say, this is causal?
MR. MURDICA: Objection to form.
THE WITNESS: Not to my knowledge. I think there's some ones that are interesting markers, but not in and of themselves supportive of a causal link.
QUESTIONS BY MR. SNIDOW:
Q. How about valproic acid?
MR. MURDICA: Objection to form.
THE WITNESS: We've talked about valproic acid. I think there is, you know, interesting and compelling data that we need to continue to evaluate.
QUESTIONS BY MR. SNIDOW:
Q. Do you think the most likely explanation for the valproic acid association with ADHD is causation?
MR. MURDICA: Objection to form.
THE WITNESS: I don't know that I can answer that yet. I think I

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would want to see more studies before I was able to really --
QUESTIONS BY MR. SNIDOW:
Q. Well, you have a section of your report on valproic acid and ADHD, right?
A. Uh-huh.
Q. Is that right?
A. I do.
Q. So you read those studies?
A. I did.
Q. All right. And based on those studies that you read, do you think that there's enough evidence to say that valproic acid causes ADHD?
MR. MURDICA: Objection to form.
THE WITNESS: So, again, I would never say an individual agent causes ASD or ADHD.
QUESTIONS BY MR. SNIDOW:
Q. Oh, never?
MR. MURDICA: Objection to form.
THE WITNESS: I would not say on the basis of the data on valproic

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acid that there is a causal association because it's observational data, and we have to always take into account the potential for bias, the potential for genetic confounding, the potential for confounding by indication, all of the things that we've talked about.

QUESTIONS BY MR. SNIDOW:

Q. Okay. You think that scientists should keep studying the association between prenatal APAP exposure and ADHD?

A. So I imagine that there are people that have data that might be relevant to the question at hand. I would never say, don't analyze data that exists that might help to resolve what appears to be an ongoing debate about whether there is any causal association.

And the value of additional publications and data, in my mind, would be the public health value, the benefit to pregnant women who experience pain or difficulty sleeping or whatever the case may

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be for whom APAP is an effective and safe medication.

And so it would be very nice for women not to have to worry about that during pregnancy.

Q. Yeah.

A. That would be the value of additional studies, in my mind.

Q. You mentioned the ongoing debate about whether it's causal or not.

Do you know any of the epidemiologists on the other side of that debate that think it is causal?

A. Not personally.

Q. Okay. Do you have any reason to think that the people on the other side of the debate, about whether it's causal or not, are bad epidemiologists?

MR. MURDICA: Objection to form.

THE WITNESS: Again, if you asked me about a specific person, I -- you know, I don't know everyone's record. I don't know enough about those individuals to opine about their

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integrity or their career.

QUESTIONS BY MR. SNIDOW:

Q. Sure.

When you -- when you saw their names, did any of them jump out to you and say, oh, that's a -- he's a known quack who works in this field?

MR. MURDICA: Objection to form.

THE WITNESS: I don't typically think of people as quacks or non-quacks.

QUESTIONS BY MR. SNIDOW:

Q. Yeah.

A. And so I look at their career, and I can make a judgment based on that, but I don't have any specific response to the individuals who are involved in this litigation.

Q. In this debate. I meant in the broader literature.

MR. MURDICA: Objection to the form.

THE WITNESS: Again, I don't have an opinion.

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QUESTIONS BY MR. SNIDOW:

Q. When you saw the names of the epidemiologists on the other side of the debate about whether acetaminophen causes autism, did you -- did you see any of them and say, ah, I've actually noticed they published bad studies in the past?

MR. MURDICA: Objection to the form.

THE WITNESS: I didn't evaluate them with that eye, but it didn't -- it didn't strike me that way.

QUESTIONS BY MR. SNIDOW:

Q. Okay. Do you think as of now we can say with certainty that there's no causal relationship between prenatal APAP exposure and ASD?

A. I do.

Q. You can say it with certainty?

A. I think that based on the body of evidence that exists today, there is no peer-reviewed, published epidemiologic evidence to support a causal association between acetaminophen and ADHD or A -- or ASD in the offspring.

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Q. That's a little different. I'm not actually asking about the body of literature.

I'm saying, are you certain that there is no causal relationship between prenatal APAP exposure and ASD?

A. I understand that that's what you're asking me.

Q. Okay.

A. My only way to evaluate and answer that question is based on the existing body of literature. I'm an epidemiologist. That's what I was asked to do in this litigation, and that's what I've done. And that's what my opinion is based on.

Q. Right.

But I'm saying -- let me ask it a different way.

Did any of the papers that you reviewed have the conclusion, based on our study, we now know for sure that APAP does not cause ASD? Any of them say that?

MR. MURDICA: Objection to the form.

THE WITNESS: I don't think

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that any epidemiologist would make a conclusion like that based on a single study, which is what they've authored.

QUESTIONS BY MR. SNIDOW:

Q. Well, how about the ones who did like meta-analysis or literature reviews, you read those too, right?

A. I did read those.

Q. And did any of them say, I've read the literature and I can say with 100 percent certainty that prenatal APAP exposure doesn't cause autism?

A. Again, I don't believe a credible epidemiologist would ever state an opinion like that.

I will tell you what the meta-analyses' authors did say which is, we can't determine because there is so many potential confounders and biases in this literature.

Q. Okay. Did any of the papers you reviewed say, based on the data in this study, we're sure that this association is entirely spurious?

A. Again, I don't think a credible

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epidemiologist would ever make a statement like that in a paper. When you are writing a manuscript, you're using the body of data that you have for that paper, for that analysis. It's a single analysis or a set of analyses, and we don't determine yes or no.

Epidemiology is an iterative science, as I've said in my report, and we build evidence over time, and that is why we need to use a set of criteria to evaluate that body of evidence at the end.

Q. Did any of the papers that you reviewed state an opinion that there is no risk to the developing fetus from prenatal APAP exposure? Any of them say that?

A. I would have to review the articles to see if that was a statement that any of them made. I -- I can't just recall that off the top of my head.

Q. None of them come to mind, though, right?

MR. MURDICA: Objection to form.

THE WITNESS: Again, I would want to review the studies and

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evaluate the statements they made in the context of their assessment of their data and their discussion of that data and the limitations of that data and the interpretation of that data.

QUESTIONS BY MR. SNIDOW:

Q. Yeah.

Any studies in the literature say that the consistency factor of Bradford Hill is not satisfied when looking at the overall literature?

A. Again, I --

MR. MURDICA: Objection to form.

THE WITNESS: I -- so that would be a meta-analysis I would -- I would imagine. You wouldn't do that in an individual study because we apply Bradford Hill to a set of studies.

And again, I don't recall from the meta-analyses what the specific findings with respect to the Bradford Hill criteria were, but I'd be happy

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to look through them, if you want me to.
QUESTIONS BY MR. SNIDOW:
Q. No, that's fine. If you don't remember.
And the same question for any of the other Bradford Hill criteria, did any of the studies they reviewed say, this factor of Bradford Hill is not satisfied for this literature?
MR. MURDICA: Objection. Form.
THE WITNESS: I would review the meta-analyses for those specific statements. I don't recall offhand whether any of them were willing to say that, but -- able to say that.
QUESTIONS BY MR. SNIDOW:
Q. I assume you think that the APAP label should not warn about the risk of autism or ADHD?
MR. MURDICA: Objection to the form.
THE WITNESS: I have no opinion about the label. That's not what I was asked to review, and I have never

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seen it.
I mean, maybe I've seen it, but it's not something that I reviewed as part of this engagement.
QUESTIONS BY MR. SNIDOW:
Q. Well, do you think it would be a truthful statement to put on the label that some studies have shown that prenatal APAP exposure causes autism?
MR. MURDICA: Objection to form.
QUESTIONS BY MR. SNIDOW:
Q. I'm sorry, is associated with autism?
MR. MURDICA: Objection to the form.
THE WITNESS: Again, that's not my area of expertise. I was not asked to opine on the label, and I don't have an opinion based on my expert evaluation of the literature.
QUESTIONS BY MR. SNIDOW:
Q. Would that be a true statement, though, some studies have shown that prenatal APAP exposure increases the risk of autism?

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MR. MURDICA: Same objection.
THE WITNESS: Again, we're talking about the label, and it's not something that I'm willing to opine on.
QUESTIONS BY MR. SNIDOW:
Q. Put the label aside.
If I said some studies have shown an association between prenatal APAP exposure and autism, is that true or false?
MR. MURDICA: Objection to the form.
THE WITNESS: So that's a very general statement that comes out of nowhere, and I don't know who the audience is. I don't know what studies you're considering. I can't agree or disagree to a statement like that.
QUESTIONS BY MR. SNIDOW:
Q. You can't agree or disagree whether some studies have shown an association between prenatal APAP exposure and autism?
MR. MURDICA: Objection to the

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form.
THE WITNESS: I would want to know what the "some studies" are.
QUESTIONS BY MR. SNIDOW:
Q. I know, but that's all I'm saying. They exist, don't they?
MR. MURDICA: Objection to form.
THE WITNESS: Again, I would want to be specific in my response. I'm not willing to make a general statement like that.
MR. SNIDOW: Can I have the ELMO, please?
Jim, you can have an objection to my demonstrative.
Okay?
QUESTIONS BY MR. SNIDOW:
Q. I pulled this from page 17 of your report.
Look familiar?
And I'll tell you what I did to it in a second. But do you see on page 17 --
A. It looks a little different than what I'm -- yeah.

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Q. So you've made it general. I've just made it specific to this case.
But you agree this is -- this accurately describes what you're suggesting when you're talking about confounding?
A. Yes.
Q. Okay. And I made one for autism, and I made one for ADHD.
A. Okay.
Q. Okay. And you think that this is what's going on here. You think there's a confounder that's associated with prenatal APAP use and autism?
A. Correct.
MR. MURDICA: Objection to form.
QUESTIONS BY MR. SNIDOW:
Q. Now, for this to be a confounder, you agree the confounder has to cause autism, right?
MR. MURDICA: Objection to form.
THE WITNESS: The confounder has to be associated with autism.

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QUESTIONS BY MR. SNIDOW:
Q. All right. We'll get to that to -- in a second. But for now, confounder has to be associated with autism, right?
A. Uh-huh.
Q. And the confounder has to be associated with prenatal APAP use.
A. That's the definition of a confounding variable.
Q. All right. So for this association, tell me, what should I write here for confounding variables? I know genetics is one of them, right?
MR. MURDICA: Objection to form.
THE WITNESS: Genetics.
QUESTIONS BY MR. SNIDOW:
Q. All right. Any other ones?
A. Indication for use.
Q. Okay. Uh-huh.
Any other ones?
A. I'm going to leave it at that for confounding variable.
Q. Okay. And for ADHD, should I

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write genetics again?
A. You should.
Q. And indication?
A. Uh-huh.
Q. And indication is whether the mother's using it for fever or pain and so on?
A. It's the indication for the use of acetaminophen, correct.
Q. All right. So for autism, what evidence -- what paper suggests that the genes of the mother that cause autism or associated with autism are associated with prenatal APAP use?
MR. MURDICA: Objection to the form.
THE WITNESS: So because we don't understand all of the genetic contribution, the specific genes that cause autism, no one has been able to directly study that.
QUESTIONS BY MR. SNIDOW:
Q. Okay. All right. That's fine. So --
MR. MURDICA: She was going to

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continue answering, and you interrupted her. Please don't do that.
THE WITNESS: So because we don't know the specifics of the genes that cause autism and we, therefore, can't test for them to see if they are a specific confounder, what we have done is used statistical techniques to assess whether genes might play a role.
QUESTIONS BY MR. SNIDOW:
Q. Right.
What paper is that?
A. In the -- in the autism literature, there is not a study that has done what I would consider the best control for genetics, which would be a sibling control, and so we don't have sufficient evidence to really support that as a -- as a confounding variable and yet, because of what we know about autism and its genetic components, we can be sure that it is a potential confounder.
And, you know, we talk about

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potential confounder, and then we test to see if it's there.
Q. All right. So you said we don't have sufficient evidence.
Okay?
MR. MURDICA: I don't hear a question.
MR. SNIDOW: No, no, no. Nope. You can have the objection.
MR. MURDICA: Well, there is no question.
MR. SNIDOW: I'm going to turn to the next one.
That's fine. I'll ask one.
So here's one --
MR. MURDICA: You can't just write stuff down that she didn't say.
MR. SNIDOW: She absolutely said it.
MR. MURDICA: You can't take it out of context.
MR. SNIDOW: There's a transcript. There's a transcript.
QUESTIONS BY MR. SNIDOW:
Q. This is the one for ADHD.

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So you agree for it to be a confounder, the confounder has to be associated with prenatal APAP use, right?
A. Correct.
Q. What evidence is there that genetics that determine ADHD are associated with prenatal APAP use?
A. So we have studies that have evaluated both the polygenic risk score and maternal psychiatric issues and their propensity to ingest acetaminophen during pregnancy.
And they support the association that the women who have that propensity for autism, whether it be through PRS or through report of their own psychiatric history --
Q. Yeah.
A. -- are more likely to use APAP during pregnancy than women who do not.
Q. And that study is called Leppart, right?
A. Right.
Q. So I'm going to write Leppart here, and that's 2019, right?

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A. Uh-huh.
Q. And that was a PRS study, right?
A. Correct.
Q. And it looked at a polygenic risk score, which ones were associated with ADHD, and then looked at whether it was associated with acetaminophen, right?
A. Uh-huh.
Q. Okay. What did the Leppart study show for autism?
A. So the Leppart study for autism, I would want to review specifically.
Q. Okay. Yeah. That's fine.
A. So I am sure to state the correct numbers. Okay?
MR. MURDICA: Are you providing it to her? Is that what you're doing?
MR. SNIDOW: No, she's showing me. She's got it.
THE WITNESS: I'm sorry?
QUESTIONS BY MR. SNIDOW:
Q. Are you looking at your report? What are you looking at?
A. I was going to look at my

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report, but I can also look at the study itself, and that's probably what I'll do.
Q. Yeah. All right.
A. I just want to make sure I cite the numbers correctly.
(Pinto-Martin Exhibit 607 marked for identification.)
QUESTIONS BY MR. SNIDOW:
Q. So this will be 607, which is tab JJ for me.
MR. SNIDOW: There you go. Are you going to want this?
MR. MURDICA: Yes. Thank you.
QUESTIONS BY MR. SNIDOW:
Q. All right. And if you turn to 838.
Do you see that?
A. Uh-huh.
Q. No association, right, for autism?
A. So we're looking at Table 3?
Q. Uh-huh. No, 2.
A. Okay. We're looking at Table 2. ASD, PRS and acetaminophen. They report -- they do not report a statistically

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significant association, that's correct.
Q. Almost -- I mean, almost exactly null, right?
A. I would say the first one is -- yeah, is null and the second one is very close to null.
Q. Okay. So I'm going to write Leppart, no association.
A. And I would like to point out that a polygenic risk score does not capture the entire universe of genetic risk because we, as I said before, don't understand all of the genes that cause or interact to cause autism.
Q. Right.
But if I asked, is there -- what affirmative evidence is there that prenatal APAP use is associated with the genes that cause autism, the answer is, all we have is Leppart, and there's no association, right?
MR. MURDICA: Objection to form.
THE WITNESS: Again, I think it's -- when you have imperfect

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information and you don't find an association, it doesn't mean that the association doesn't exist. It means you were not able to find it on the basis of the data that you have.
QUESTIONS BY MR. SNIDOW:
Q. Okay. For -- you still have Leppart up?
A. I will.
Q. Yeah.
A. Yeah.
Q. Okay. For autism -- ADHD. Sorry, for ADHD. You see in Table 2 where it reports an association?
A. Yes.
Q. In Leppart here, this is what you told me was the evidence that the genes associated with ADHD are associated with prenatal APAP use, right?
MR. MURDICA: Objection to form.
THE WITNESS: This is one piece of evidence in support of that confounder, yes.

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QUESTIONS BY MR. SNIDOW:
Q. All right. What else is there?
A. Well, I'm just saying there is one piece of evidence. I'm not -- I'm not saying there's another one. I'm saying this is one piece of evidence.
Q. I know.
But you're not aware of anything else other than Leppart, right?
MR. MURDICA: Objection to form.
THE WITNESS: I believe that the ALSPAC cohort also had some data, but I would want to remind myself of the specifics of that.
QUESTIONS BY MR. SNIDOW:
Q. All right. We'll do that in a second.
So for Leppart, would you -- the results they showed was there was a risks -- odds ratio of 1.09?
A. Right.
Q. And then 1.11?
A. Right.
Q. And the confidence intervals

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are really close to 1, right?
A. What do you mean by that?
Q. They're 1.02 --
A. The lower band of the confidence interval?
Q. Yeah. Yeah.
A. Yeah.
Q. And you would characterize that as barely statistically significant?
A. I have characterized it as that in the past.
Q. Yeah.
And you would characterize those odds ratios as weak, right?
A. I don't know that I would ever call an odds ratio weak, but they are not, you know, incredibly powerful.
Again, remembering that what the PRS captures is just a fraction of the overall genetic risk. So the fact that they found anything is actually quite compelling.
Q. Okay. All right.
Do you have -- do you see any evidence that a mother's use of acetaminophen before she gets pregnant causes autism?

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A. So there have been some attempts to do what we call a negative control exposure analysis to look at that very question, does prenatal use --
Q. Pre-prenatal use.
A. Pre-prenatal use. I'm sorry.
Q. Yeah.
A. Prepregnancy use.
Q. Yeah.
A. -- increase the risk of autism or post-pregnancy use increase the risk of autism.
Q. Yeah.
A. And several authors have used that design to -- in an attempt to show that it's an intrauterine effect.
Q. Yeah.
A. However, there are instances in this literature where the opposite was found. In fact, they showed that prepregnancy use and post-pregnancy use did have an association, which would argue for an underlying genetic or familial risk.
Q. With autism diagnosis?
A. Yes.

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Q. And what study is that?
A. I'll have to go to my report to remind myself.
Q. Sorry. Just to be clear, I'm asking you, you're telling me there's a study that looked at prepregnancy use and found an association with autism diagnosis?
A. I need to go to my report to remind myself.
Q. All right.
A. There's so many studies --
Q. Let's move on. At a break, I'd like you to do that.
A. Okay.
Q. And the same question for ADHD. Do you think that there are studies that looked at prepregnancy use? Yeah, you do.
And I'm talking about ADHD diagnosis.
A. Correct.
Q. Okay. Not any of the screening tools.
A. Well, again, I would want to review my report to make sure those are the studies that I'm talking about.

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Q. Yeah.
A. There's five studies that used ASD diagnosis as an outcome, and eight or nine, depending on how you count, and then there are many, many others that used other outcomes.
So I would want to look specifically at the studies before I answered the question.
Q. All right. Why don't you do that on a break, and we'll come back to it.
Put that aside for now.
Okay. On page 74 of your report, you have a table of results in the literature looking at ADHD diagnosis, right?
A. Correct.
Q. And you chose which results to put in this table, I think?
A. I did.
Q. And did you make a forest plot of those results?
A. No.
Q. No.
Well, I did. Let me show you what it looks like. All right.

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MR. MURDICA: Note my objection to the use of the demonstrative created by the plaintiff's lawyer.
MR. SNIDOW: That's fine. That's fine.
MR. MURDICA: You don't need to tell me it's fine. I'm making my objection.
MR. WATTS: Overruled.
QUESTIONS BY MR. SNIDOW:
Q. Dr. Pinto-Martin, I'm not asking you to check every one, but take a look at the table 70 -- on 74 and 75, and let me know if you see any obvious errors in what I've done here.
And I'll tell you one. Obviously, the Ystrom, the upper bound confidence interval, needs to go way, way up. I just did that so the paper wouldn't be so long.
A. Sorry, I'm just checking to make sure these are accurate.
Q. Yeah.
A. So I haven't checked every single one, but the ones I've looked at so

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far --
Q. Looks pretty good?
A. Yeah.
Q. Okay. And you chose these results, right, to include in your table?
A. I did.
Q. Yeah. If you turn -- I'm going to turn to the next page, which all I've done is, do you see how there's one to seven days and less than eight days in Ystrom and Gustavson?
A. Uh-huh.
Q. I've taken those off just to show the longer-term results because -- otherwise, it's the same chart.
All right?
A. Okay.
Q. All right. So looking at this study, do you agree that 100 percent of the results here for long-term use of prenatal APAP show a positive point estimate for the risk of ADHD diagnosis?
MR. MURDICA: Objection to the form and use of the demonstrative.
THE WITNESS: So when you say

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"looking at the study," I think you mean looking at this chart that you created?
QUESTIONS BY MR. SNIDOW:
Q. Yep. Sorry. Yes.
A. So I disagree because there are two or three that show a nonsignificant association.
Q. You know what a point estimate is, right?
A. Right. Oh, I'm sorry, is that what you asked about?
Q. Yeah. Can I ask it again?
A. So I -- yeah.
Q. Do you agree that 100 percent of these studies had a point estimate showing a positive association between prenatal APAP exposure and the risk of ADHD diagnosis?
A. So --
MR. MURDICA: Objection to form.
THE WITNESS: -- I will say that I agree with that statement, and I would immediately qualify it by saying that a point estimate taken in

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isolation is meaningless in my mind.
First of all, we need to look at the statistical significance and the confidence interval associated with that point estimate, and we have to think about the data upon which that point estimate is based.
QUESTIONS BY MR. SNIDOW:
Q. Sure.
So let's do the first one first.
This one is statistically significant, right?
MR. MURDICA: Objection. Form.
THE WITNESS: I'm sorry, which --
QUESTIONS BY MR. SNIDOW:
Q. This one.
A. You're pointing to greater than 29 days?
Q. Yep.
A. That study reported a statistically significant result for greater than 29 days --
Q. Okay.

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A. -- which they then demonstrated was confounded by genetics, and when they did the sibling control, it was null.
Q. Okay. We'll get there. And I included it. I included the sibling control for you, right?
A. I see it, but you were about to jump over it.
Q. No. No.
A. I wanted to point that out.
Q. I just wanted to say which one was statistically significant. This one is?
A. That report of two trimesters of use in the Gustavson 2021 has a significant point estimate.
Q. Okay.
A. However, I think we need to really characterize the data that drives that. They are talking about trimesters of use here based on maternal recall, and it is recall, of use of APAP in the prior trimester of their pregnancy. And they are then using that to derive trimester-specific estimates.
So I would say that these data are very fragile and not particularly

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compelling with respect to exposure.
Q. Okay. That's fine. But I'm actually just asking about statistical significance, and there's one, two, three, four, five, six, seven, eight, nine -- ten more, right?
MR. MURDICA: Objection to form.
THE WITNESS: There are ten point estimates there that are statistically significant, and each one of them needs to be evaluated in the context of the study from which it was derived and the data that supports that purported statistically significant association.
QUESTIONS BY MR. SNIDOW:
Q. Yeah.
And just to get the record clear, there's actually one, two, three -- sorry. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12 -- 13, right?
MR. MURDICA: Objection to form.
THE WITNESS: Again, there are

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13 point estimates that are statistically significant according to the evaluation done by the authors in those studies.
Those authors themselves often contextualize that result to indicate that there are potential confounders and biases that could be driving the result.
QUESTIONS BY MR. SNIDOW:
Q. So my question is, you say in your report that you think that these results could be due to chance.
Is that right?
MR. MURDICA: Objection to the form.
THE WITNESS: I don't recall in my report where I might have said that. It's certainly possible that that is one explanation for some of these findings --
QUESTIONS BY MR. SNIDOW:
Q. Okay.
A. -- because many of them analyzed a multitude of specific outcomes,

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for example, on a screening questionnaire, individual items, sub-scales.
So they are looking at many, many, many outcomes and at times not adjusting for the multiple testing, which could result in a type 1 error.
Q. Right.
A. So when I talk about chance, that's what I'm referring to.
Q. And that's actually helpful.
I wanted to clarify, though, you're not suggesting that you can get 13 statistically significant results in a row due to chance, are you?
MR. MURDICA: Objection to the form.
THE WITNESS: I don't believe I said that anywhere in my report.
QUESTIONS BY MR. SNIDOW:
Q. And you don't think that?
MR. MURDICA: Objection to form.
THE WITNESS: I can't answer that without looking specifically at each individual study and saying, is

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there a chance that chance explains this finding in this study, in this study. I can't do it as a whole.
QUESTIONS BY MR. SNIDOW:
Q. Well, you know that the chance is going to be less than .05 for all the ones that are statistically significant, right?
A. That's right.
Q. Okay. So the chance of a chance finding -- sorry, there's no way around chancing?
A. I know.
Q. Yeah. The chance of a chance finding for this result is .05?
A. Correct. But look what happened once they did the sibling control, sir.
Q. No, we're talking about chance right now.
MR. MURDICA: It -- well, hang on. You can't do that.
MR. SNIDOW: Okay.
MR. MURDICA: You can't -- you can't wave her off. You can't interrupt her. That is not

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appropriate deposition conduct.
You can't wave me off either, J.J. You just did what you did, and you can't do that. That is improper deposition conduct. Please conduct yourself appropriately.
QUESTIONS BY MR. SNIDOW:
Q. The chance of a chance finding for this result is less than .5, .05?
A. Less than .05, correct, as reported in that study with the caveat that we need to understand exactly where these data were derived and what they --
Q. But the odds of that happening twice, .05, .05 -- it's what, .0025?
MR. MURDICA: Objection to the form.
THE WITNESS: I'm not sure that you can take the chance estimate from one study and apply it to another study and say that, you know, there's a doubling of -- a decrease by 100 percent of that chance.
I don't -- I -- we do chance finding within an individual study,

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within an individual analysis. That's the way it's done.
QUESTIONS BY MR. SNIDOW:
Q. All right. What's the odds of flipping a head when you flip a coin?
A. 50/50.
Q. And what's the odds of doing that twice?
A. 50/50.
Q. Right.
And what's the -- no. What's the odds of it happening twice, heads, heads?
A. Oh.
Q. Yeah, okay. Well, I'll tell you, it's .25, because you multiply the probabilities together, right?
MR. MURDICA: Objection to the --
THE WITNESS: You're talking about flipping a coin. I'm talking about an epidemiologic study that has, you know, all other kinds of things that we need to address when we're looking at the result.

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QUESTIONS BY MR. SNIDOW:
Q. Did you do a calculation, though, to see what the likelihood of all of these being due to chance was?
MR. MURDICA: Objection to the form.
THE WITNESS: Again, that is not my primary objection with these studies that have ASD as -- ASD or ADHD in this case as an outcome.
The bias -- I mean, the chance finding was primarily directed at the studies that used screening tools as an outcome because of what we talked about before and the multiple testing and the likelihood of chance finding there.
QUESTIONS BY MR. SNIDOW:
Q. All right. So the chance was not your primary objection?
MR. MURDICA: Objection to the form.
THE WITNESS: With respect to the studies that had ADHD as an outcome --

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QUESTIONS BY MR. SNIDOW:
Q. Yeah.
A. -- diagnostic outcome, chance was not my primary objection to the credibility of the results where there was a reported increased risk.
Rather, it was based on the imprecision of the exposure, which is extremely important when we're talking about fetal brain development, and we need to think about the timing and the dose and the duration of exposure in order to be able to assess whether that exposure actually had an increased risk on the likelihood of autism in the offspring.
Q. All right. Could you turn to page 93 in your report?
A. (Witness complies.)
Q. All right. And do you see where you say, "A Bradford Hill analysis is only called for when the epidemiological literature establishes an association that is perfectly clearcut"?
A. I do.
Q. And then you say that you don't

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actually think that you should be doing a Bradford Hill analysis of the ADHD literature at all, right?

A. This is ASD, but, yes.

Q. Yeah.

And the reason why you say that is because you don't think that there's an association in the literature at all between prenatal APAP use and ADHD, right?

A. I don't believe there's a cred -- there's credible evidence of an association between prenatal APAP use and ASD.

Q. Well, how many studies -- how many studies have to go on the forest plot before you at least concede there's an association?

I mean, look, confounding I get, but how many do you need before you get an association?

MR. MURDICA: Objection to the commentary.

THE WITNESS: Well, I would say confounding you don't get because that's exactly the point here. We

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could have thousands of estimates of an elevated risk, and if they're all confounded, then in my mind that does not equate with strength of an association.

It's not about a number. It's not about counting. It's about evaluating each individual study and the strength of the data that drives the point estimate that they report.

I don't believe we have that here.

QUESTIONS BY MR. SNIDOW:

Q. Well, I agree. It's just not what you said in your report, right?

You said you don't think there's an association because it's not, quote, "Perfectly clearcut and beyond what we would care to attribute to the play of chance."

Is that what you said?

MR. MURDICA: Objection to the form of the question.

THE WITNESS: I didn't say that. Bradford -- Dr. Hill said that.

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QUESTIONS BY MR. SNIDOW:

Q. No, no, no. You said, "In my opinion, the literature has not identified an association that's perfectly clearcut and beyond what we would care to attribute to the play of chance."

Right? You said that?

MR. MURDICA: Objection to form to the form of the question.

You can answer it.

THE WITNESS: So I put "perfectly clearcut" in quotes because that is a direct quote from Hill, who established the Bradford Hill criteria, and said in the absence of a perfectly clearcut association between an exposure and an outcome, Bradford Hill is not warranted.

QUESTIONS BY MR. SNIDOW:

Q. Uh-huh.

And so my question is this, do you think that these results are beyond what you would care to attribute to the play of chance?

MR. MURDICA: Objection to the

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form.

THE WITNESS: So, again, we're not talking just about chance here. We're talking about the criteria of Bradford Hill, and what goes into that evaluation includes all of the things that I mentioned before: The context of the studies, the sample size, the selection bias, the assessment of exposure.

All of those things matter when we're trying to establish a, quote/unquote, clearcut association.

Because of the problems in these studies, the methodologic problems, I do not believe we've established a clearcut association.

QUESTIONS BY MR. SNIDOW:

Q. My question is, do you think these could all be due to chance? That's my only question.

MR. MURDICA: Objection to the form.

THE WITNESS: Again, we would have to look at each study

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individually to say whether chance might be an explanation for the finding. I can't do them as a whole.
QUESTIONS BY MR. SNIDOW:
Q. Okay. You've read the consensus statement, right?
A. Uh-huh.
Q. And did you know any of the authors?
A. Not personally.
Q. Any professionally?
A. So Dr. Swan was a biostatistician professor when I did my doctorate at Penn -- I mean, not at Penn, I'm sorry -- at the University of California-Berkeley.
Q. Did you work with her?
A. She wouldn't remember me, I'm sure.
Q. She wouldn't remember you?
A. No. I was one student in a class.
Q. But you took her class?
A. I did.
Q. Do you think she's an

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unreasonable epidemiologist?
A. She's a biostatistician. I think she's, you know, a solid biostatistician from my experience with her in class.
Q. And she's one of the lead authors on that consensus statement?
MR. MURDICA: Objection to the form.
THE WITNESS: I believe so. I'm not sure exactly where she is in the authorship, but...
QUESTIONS BY MR. SNIDOW:
Q. What is -- are you aware that society for Pediatric and Perinatal Epidemiological Research, SPER, gives out an award each year?
MR. MURDICA: Objection to the form.
THE WITNESS: I recall that, yeah. Well, they give out several awards. They give out a student award. They give out a best paper award.

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QUESTIONS BY MR. SNIDOW:
Q. Yep.
A. Oh, yeah.
Q. Rising star award?
A. Yeah.
Q. Do you remember that one?
A. I've heard of it, yeah.
Q. And do they typically give that one to good epidemiologists?
MR. MURDICA: Objection to form.
THE WITNESS: I have no knowledge of, you know, who evaluates that rising star, but I would imagine that they look at the individual carefully.
QUESTIONS BY MR. SNIDOW:
Q. Yeah.
And again, you were present at SPER, right?
A. I was, back when it was first formed.
Q. Outstanding organization of epidemiologists, correct?
A. It's a good organization.

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MR. SNIDOW: Can I have YYY? Thanks.
QUESTIONS BY MR. SNIDOW:
Q. While she's getting that, do you know who Zeyan Liew is?
A. I do not, except from reviewing the literature. I've never --
Q. But you see his name in the literature?
A. I've seen his name, yes.
Q. He's in a lot of it, right?
MR. MURDICA: Objection to form.
THE WITNESS: He's written a lot of studies, yes.
QUESTIONS BY MR. SNIDOW:
Q. There's Liew 2014.
A. 16, ABC.
Q. Exactly.
A. 19, yes.
Q. Yep.
And Olsen and Liew 2017?
A. I guess I think of '16 as ABC. Maybe you're thinking C is '17.
Q. Olsen and Liew, 2017?

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A. Oh, Olsen and Liew, yeah, different paper, yeah.
Q. All right. So half a dozen studies directly on this question, right?
MR. MURDICA: Objection to the form.
THE WITNESS: He's written many studies on this, yes. He's written many papers. He hasn't done a study himself, but he's used data.
(Pinto-Martin Exhibit 608 marked for identification.)
QUESTIONS BY MR. SNIDOW:
Q. All right. So I'm going to show you a printout of the SPER website. We'll mark it 608.
And if you look down --
MR. MURDICA: Do you have mine?
MR. SNIDOW: I do not.
MR. MURDICA: Thank you.
QUESTIONS BY MR. SNIDOW:
Q. If you look down under 2020, do you see that in 2020 they gave an honorable mention for the rising star award to Zeyan Liew?

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A. I do see that.
Q. In 2020, that was after he had published all of the studies that we just talked through?
A. That's correct.
Q. And you know that he studies acetaminophen fetal development pretty much full-time, right?
MR. MURDICA: Objection to form.
THE WITNESS: I know nothing about what Zeyan Liew does.
QUESTIONS BY MR. SNIDOW:
Q. Okay.
A. But I know that he publishes studies.
Q. You know he's a primary author on the consensus statement?
MR. MURDICA: Objection to the form.
THE WITNESS: I know he was an author. I don't know where he is in the author list.
QUESTIONS BY MR. SNIDOW:
Q. And then after he wrote all of

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those papers in 2020, SPER gave him honorable mention for the Rising Star Award?
A. That looks to be the case.
Q. You mentioned Dr. Swan?
A. Swan, Shanna Swan.
Q. Shanna Swan.
A. Uh-huh.
Q. Yeah. Do you think that reasonable scientists could sign on to the consensus statement?
A. I do think reasonable scientists could sign on to the consensus statement because it's not -- it's not a study. It's an interpretation of the literature that some people will feel one way about and others will feel another way about.
So reasonable scientists could disagree. Some could agree to sign on. Some could say no thank you.
Q. Sure.
The consensus statement recommends that women be warned about prenatal acetaminophen use?
A. They believe that the precautionary principle should be applied

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here. Although they admit that the data is still quite flawed and needs to be further evaluated, they believe that the precautionary principle should be applied. That is what they said.
Q. And do you think that's a reasonable view?
MR. MURDICA: Objection to the form.
THE WITNESS: I actually disagree with that view.
QUESTIONS BY MR. SNIDOW:
Q. Okay.
A. Because I think that the risk of denying women a pain medication during pregnancy is a significant one from a public health perspective, and I think that they overstepped the bounds of the literature that they reviewed.
Remember, they did not do any of their own study or analysis. They just summarized some of the literature that existed at the time.
Q. I get that you disagree, and it's kind of uncertain, but do you think it's

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reasonable for them to have recommended that?
MR. MURDICA: Objection to the form.
THE WITNESS: I believe I answered that already, and I don't agree with that. I would not have signed on to that statement. I think that --
QUESTIONS BY MR. SNIDOW:
Q. Not asking you -- sorry. Not asking you for your personal opinion.
What I'm saying -- let me put it a different way.
Do you think that they were being unscientific when they made that recommendation?
MR. MURDICA: Objection to the form.
THE WITNESS: I'm not sure what you mean by "unscientific." They are not evaluating primary data and saying, "This is what these data show." They're interpreting the literature that existed at the time and saying, "We think we should have

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applied a precautionary principle here," which is their language --
QUESTIONS BY MR. SNIDOW:
Q. Yeah.
A. -- which really means going beyond what the data shows and taking a stand based on what we believe the interpretation of that data should be.
Q. Yeah.
MR. MURDICA: And when you're done with this area and there's not a question pending, J.J., we've been going an hour. It's up to you.
MR. SNIDOW: Okay.
Go off the record?
MR. MURDICA: Yeah.
MR. SNIDOW: Okay.
THE WITNESS: Break? Okay.
VIDEOGRAPHER: The time is 11:11 a.m., and we're off the record.
(Off the record at 11:11 a.m.)
VIDEOGRAPHER: The time is 11:23 a.m., and we're on the record.
QUESTIONS BY MR. SNIDOW:
Q. Okay. Dr. Pinto-Martin, during

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the break, were you ever able to tell me what studies showed that prepregnancy use of acetaminophen is associated with autism diagnoses?
A. I'm sorry, I didn't look at that.
Q. Okay. Will you do that next?
A. I'm happy to do it when we have a longer break.
MR. MURDICA: Object to form.
No, you don't have to do anything during the break. Nobody tells you what to do.
You can ask your questions.
QUESTIONS BY MR. SNIDOW:
Q. If you would, I would appreciate it.
MR. MURDICA: No. Objection. That is not how depositions work.
J.J., you can ask questions if you want. Don't tell anybody what you appreciate or what you wouldn't appreciate.
If you want to use your time that way, use it.

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QUESTIONS BY MR. SNIDOW:
Q. Have you ever published your view of the evidence between prenatal acetaminophen exposure and autism?
A. I have not published on this question, no.
Q. So you -- have you given a lecture on it?
A. No.
Q. Letter to the editor?
A. No.
Q. You can do that when you disagree with a study, right?
A. You can do that when you disagree with a study, yes.
Q. An editorial in a journal?
A. I've not done anything, no.
Q. Asked to speak at a conference?
A. No.
Q. Told any professional peers?
A. No.
Q. Written to any authors of these journals?
A. I have not.
Q. Written to anyone on the

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consensus statement telling them that they're wrong?
A. I have not.
Q. And why have you decided not to get into this debate about whether it's causal?
MR. MURDICA: Objection to the form.
THE WITNESS: So I've been very occupied reviewing this literature and writing my expert report. I am not ruling out the possibility that I might write something at some point or give a lecture on it at some point.
It's not been a focus of the last, you know, six months of my life.
QUESTIONS BY MR. SNIDOW:
Q. Okay. Have you done anything to make your view -- make clear your view that APAP does not cause autism besides serving as an expert in this case?
A. I have not. And, again, I'm not ruling out the possibility that I would do that at some point in time, but it has not been the focus of my life --

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Q. Okay.
A. -- for the past.
Q. You're not a regulatory expert?
A. I am not.
Q. Not an expert on animal studies?
A. I am not.
Q. Not an expert on reviewing the literature on biological mechanisms?
A. So biological mechanisms are typically based on animal studies, and so the same answer applies. I'm not an expert in animal studies.
Q. Not an expert on biological plausibility?
MR. MURDICA: Objection to form.
THE WITNESS: So I understand the criterion of biological plausibility, and when I believe it's important to explore the literature associated with biological plausibility, I do so. But that's a -- I don't know who an expert on biological plausibility would be.

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QUESTIONS BY MR. SNIDOW:
Q. It's just something you said before, so I thought I would ask you again.
You're not a neurologist, right?
A. I am not.
Q. Not a neonatologist?
A. I am not.
Q. Not a toxicologist?
A. I am not.
Q. Not a teratologist?
A. I am not.
Q. Not a medical doctor?
A. I am not.
Q. Not a geneticist?
A. I am not.
Q. You don't do basic lab work?
A. I do not.
Q. You don't diagnose people with autism?
A. I certainly am not a clinician diagnosing people with autism, but as part of our -- the studies that I've done, I have observed probably thousands of evaluations of individuals to see if they had autism.

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Q. So, no, you don't diagnose it?
MR. MURDICA: Objection.
THE WITNESS: I do not make the diagnosis, no.
QUESTIONS BY MR. SNIDOW:
Q. And same for ADHD, you don't not diagnose them?
A. I am not a clinician. I do not make diagnoses.
Q. You also don't treat people with autism or ADHD?
A. I'm not a clinician, so I do not treat.
Q. But you're definitely an expert in autism, right?
A. I'm an epidemiologist, a peri-epidemiologist specifically, and I have spent my career studying the etiology of autism spectrum disorder.
Q. How about ADHD?
A. So ADHD is another neurodevelopmental disorder, and I have studied it in its relation to autism because the differentiation between those two and the etiology differences between those two is

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important to my work.
Q. Have you published on it?
A. There's certainly publications of mine that have ADHD in them, but it's not -- again, not my primary focus. My research has been funded to specifically look at autism spectrum disorders in the study to explore early development, which is the CDC-funded study that I've been involved in for many years. The -- one of the comparison groups is other developmental disabilities, not autism, and in that comparison group, are children with ADHD.
Q. Okay. Let's talk about confounders again for a moment.
In your report you say that the confounding variable to be a confounder needs to be independently associated with the outcome, right?
A. Correct.
Q. And you defined that as a risk factor.
A. Define what as a risk factor, I'm sorry.
Q. Whether it's independently

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associated with the outcome, you say it's a risk factor.
A. It's a potential risk factor if it's independently associated with the outcome. That's what we're exploring in an assessment of confounding.
Q. Okay. And you say that the confounder must not lie on the causal pathway between exposure and disease?
A. Correct. Correct.
Q. And do you agree it's theoretically possible that genetics predispose a woman to take acetaminophen and that the acetaminophen causes the autism?
MR. MURDICA: Objection to the form.
THE WITNESS: So I'm not sure I understand your question.
QUESTIONS BY MR. SNIDOW:
Q. All right. Hold on. Let me --
A. I think you're talking about a causal pathway.
Q. If you don't understand, let me ask again.
A. Yeah.

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Q. You say, "Must not lie on the causal pathway between exposure and disease." Right?
MR. MURDICA: Objection to the form.
And I'd appreciate it if you didn't do this hand waving thing while she's in the middle of speaking again.
Thank you.
MR. SNIDOW: Okay. I'll put my hands down.
QUESTIONS BY MR. SNIDOW:
Q. You say, "Must not lie on the causal pathway between exposure and disease," right?
A. In order for a variable to be a confounder, it cannot lie on the causal pathway between exposure and disease.
Q. And I'll give you an example.
So secondhand smoke, right?
A. Right.
Q. You know that's causally associated with lung cancer, right?
A. That has been established, yes.
Q. And there was, I think, some

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question about whether that was confounded by socioeconomic status; is that right?
A. I'm not familiar with that literature, but --
Q. Well, you talk about it in your report, don't you?
A. Yeah. I mean, I just don't know the study that you're referring to and so --
Q. Well, in your report you say it's stronger than the Tylenol literature, right?
MR. MURDICA: Objection. You cut her off again.
THE WITNESS: Can you point to me to exactly what you're talking about? Smoking and lung cancer is a stronger --
QUESTIONS BY MR. SNIDOW:
Q. Secondhand smoke. You reviewed that literature?
MR. MURDICA: Objection to the form.
Is that a question?

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QUESTIONS BY MR. SNIDOW:
Q. Yeah.
Did you review that literature?
A. I have certainly reviewed that literature in the course of my work as an epidemiologist, and I don't remember if I referred -- reviewed it specifically for this report.
Q. Okay.
A. If I referred to something, it was based on my general knowledge.
Q. Well, let me refresh your memory because you have some footnotes on it.
Can you go to page 55?
At the top there, you see you talk about secondhand smoke?
A. Uh-huh.
Q. And do you see there you say that the literature is stronger than it is for Tylenol, right?
MR. MURDICA: Objection to the form.
THE WITNESS: So I say that there were 50 consistent epidemiologic studies, and I'm now recalling that

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I -- that I looked at that in response to Dr. Baccarelli who said that, you know, a weak association can ultimately prove causal, something that I don't disagree with.
QUESTIONS BY MR. SNIDOW:
Q. Yeah.
But you do think it's stronger, don't you?
MR. MURDICA: Objection.
THE WITNESS: Stronger than what?
QUESTIONS BY MR. SNIDOW:
Q. Than the association between prenatal APAP exposure and autism, Doctor.
A. Yes, I do.
Q. Okay. And I just want to ask because I'm -- I wasn't real sure. You did look at that literature before writing this report?
A. I certainly -- when I saw that in Dr. Baccarelli's report, I went and reminded myself what was there, and I looked up a reference and cited that reference.
Q. Okay. And the reference that

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you cite is the Surgeon General, right?
A. That's correct.
MR. SNIDOW: Can I have BBBB, four Bs? It's in the back there.
QUESTIONS BY MR. SNIDOW:
Q. Okay. All right. I'm showing you an excerpt from the Surgeon General's report on secondhand smoke. It is, again, in its full version, more than -- at least 700 pages, so I've got an excerpt for you.
MR. SNIDOW: But, Jim, this one is Googleable. You can use the Google machine, as my colleague put it recently.
QUESTIONS BY MR. SNIDOW:
Q. All right. Before we look into this, Dr. Pinto-Martin, do you know what the Surgeon General's estimate for the risk ratio for secondhand smoke and lung cancer was?
A. I do not off the top of my head, but I imagine I could find it in here.
Q. Yeah, you can.
So if you go to page 434.
All right. Do you see that?
A. I see page 434, yeah.

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Q. It says, "Secondhand smoke exposure from spouses, an update in the literature, reports Hackshaw obtains a RR of 1.24."
Right?
A. I'm sorry, where are you looking? Oh, Hackshaw and colleagues pooled 1997?
Q. Yeah.
A. '97 published studies. Yep.
Q. 1.24?
A. I see that.
Q. And then they quote Zhong, 1.20?
A. Correct.
Q. Then if you turn to 436, they actually show a lot of studies.
A. Uh-huh.
Q. Do you see them there?
A. I see a whole list of studies, yeah.
Q. All right. And any of those studies show a risk ratio above 2.0?
A. Do you want me to look at them one at a time?

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Q. It should be pretty easy.
A. Not -- not that I see, no.
Q. Okay. All -- if you look down at childhood exposure?
A. I'm sorry, where is that?
Q. Childhood exposure at the bottom.
A. Oh, now we're -- oh, we're at the next page, sorry. You jumped -- got it. Oh, yeah, you're showing me here. Okay.
MR. MURDICA: No, you can look --
THE WITNESS: Okay.
QUESTIONS BY MR. SNIDOW:
Q. Do you see that?
A. Yeah.
Q. For childhood exposure, none of them are above 2.0?
A. Correct.
Q. The ones I've highlighted are statistically nonsignificant?
A. Correct.
Q. There's one of the results that shows a statistically significant protective effect, right, that Europe, six studies?

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A. Yeah.
Q. Okay. Do you still think that the relationship between secondhand smoke and lung cancer is causal?
MR. MURDICA: Objection to the form.
THE WITNESS: The data here in some instances, you've cited a bunch of different numbers and relative risks and odds ratios here.
But in general, it looks to me like the secondhand smoke exposure from spouses is consistent, and the childhood smoke exposure is less consistent.
QUESTIONS BY MR. SNIDOW:
Q. Okay. Would you say inconsistent if you looked at that?
A. So, again, as I've -- as I've described to you, my evaluation and consistency is very importantly informed by the underlying data.
And I have no idea in this set of studies here -- this is a meta-analysis, which includes many studies -- how they

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derived the exposure information, and so it's really hard for me to comment on that.
Q. But you wouldn't say that just because they had these statistically nonsignificant results, that means no causation, would you?
MR. MURDICA: Object to the form.
THE WITNESS: Again, without knowing the specifics of the study, I think we need to look carefully at what might have an impact on that, what was the sample size, how did they measure exposure.
QUESTIONS BY MR. SNIDOW:
Q. Yeah, sorry. Let me just take a step back.
You think that secondhand smoke causes lung cancer, do you not?
A. I think that there is good evidence to support a causal association between secondhand smoke and lung cancer.
Q. And you agree that many of these studies are statistically insignificant, right?

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A. Many of these studies looking at childhood exposure are statistically insignificant, yes.
Q. Well, here's the one for workplace exposure. We get two statistically insignificant results there, right?
MR. MURDICA: Object to the form, and if that's intended to be a demonstrative, to the use of the demonstrative.
QUESTIONS BY MR. SNIDOW:
Q. Is that right?
A. I see two statistically insignificant results, yes.
Q. And you still think this is a causal association, right?
MR. MURDICA: Object -- objection to the form.
THE WITNESS: I still think the weight of the evidence supports a causal association between secondhand smoke and lung cancer.
QUESTIONS BY MR. SNIDOW:
Q. Okay.
A. I think that the situation with

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secondhand smoke is a very different situation from what we have with respect to APAP in terms of the precision of the exposure.

Q. Yeah. Sure.

Let's look at the childhood one. I guess I should ask, do you think that childhood secondhand smoke exposure causes lung cancer?

A. I've never --

MR. MURDICA: Objection to the form.

THE WITNESS: Yeah. I've never reviewed that literature specifically, so I'm not willing to offer an opinion without looking at the individual studies and evaluating --

QUESTIONS BY MR. SNIDOW:

Q. Let's look at page 445 of what you've got in front of you.

Do you see the Surgeon General there, Conclusions, 1?

A. Yes.

Q. It says, "The evidence is sufficient to infer a causal relationship

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between secondhand smoke exposure and lung cancer among lifetime smokers. This conclusion extends to all secondhand smoke exposure regardless of location."

A. I see that.

Q. Okay. You can put that aside for now.

So let me ask you this. This childhood exposure forest plot, do you think that's stronger or weaker than this one?

MR. MURDICA: Objection to the form.

THE WITNESS: Again, I think just comparing point estimates across two entirely different exposures and outcomes is a misguided exercise.

QUESTIONS BY MR. SNIDOW:

Q. That's fine.

It's not just point estimates, though, right? It's confidence intervals, too?

A. Same point.

Q. Yeah, okay.

But can you tell me for the -- for the consistency of the findings, would

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you say this one is the more positive association or this one is the more consistent positive association?

MR. MURDICA: Objection to the form.

THE WITNESS: Again, you're asking me to look at two forest plots and make an evaluation that requires much more information in order to be precise about my response.

QUESTIONS BY MR. SNIDOW:

Q. Even to tell me if there's a consistent association? I'm not asking about causation.

MR. MURDICA: Same objection.

THE WITNESS: You're asking me to compare different bodies of evidence, one on smoking and one on acetaminophen. They are entirely different in the underlying data.

And I can't evaluate them with respect to their relevant consistency. I'm just not willing to do that.

QUESTIONS BY MR. SNIDOW:

Q. Right.

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But the presence of this no result here, or actually statistically significant protective effect, doesn't preclude you from making a causal inference, does it?

MR. MURDICA: Objection to the form.

THE WITNESS: I'm sorry, can you -- can you --

QUESTIONS BY MR. SNIDOW:

Q. Yeah.

A. -- rephrase that?

Q. This is the literature on childhood exposure and lung cancer, right?

A. That's what you are presenting, yes.

Q. You think it's causal, right?

A. I believe there is evidence in support of a causal association between prenatal smoking -- I mean, I'm sorry, secondhand smoking and --

Q. Yeah.

A. -- and cancer.

Q. And yet, one of the results they got was statistically significant in the

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wrong direction, right?
A. So one result from Europe, I don't know what's included there, appears to have a protective effect.
Q. And that's all I'm asking. That happens sometimes, right? Even with true causal exposure, sometimes you get a blip result, don't you?
MR. MURDICA: Objection to the form.
THE WITNESS: I don't know if it's a blip result. I don't know what the data is based on, but that is a different result from the others, I will grant you that.
QUESTIONS BY MR. SNIDOW:
Q. That's what I'm asking. Thank you.
All right. You agree that a number of people on the other side of the debate from you in this literature have said that causation is the most likely explanation?
A. So when you say "people on the other side of the debate," I'm not quite sure

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who you mean.
Q. Okay.
A. If you can give me an example of a specific person that disagrees with my conclusion, I'd be happy to --
Q. Yeah.
A. -- to think about that, but that's a broad statement, and I don't have a response.
(Pinto-Martin Exhibit 609 marked for identification.)
QUESTIONS BY MR. SNIDOW:
Q. Can I just have tab H?
Oh, gosh. All right. This, I'm going to mark, as Exhibit 609, which is Olsen and Liew 2017.
And you read this paper when writing your report, right?
A. I did.
Q. All right. If you turn to page 1395, do you see there's a paragraph that says, "The existing evidence"?
A. 1395.
Q. It's just the first page.
A. Okay.

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Q. The first --
A. Existing evidence, yeah.
Q. And it says -- and I've got the monitor if you want.
It says, "The existing evidence is based on observational data from several cohorts."
Do you agree with that?
A. I do.
Q. It says, "Different analytical options have been used."
Agree with that?
A. Uh-huh.
Q. It says, "These research findings have increased the probability that the association is causal."
Do you see that?
A. I see that.
Q. Do you agree with that one?
A. Not necessarily.
Q. Do you think it's a possibly correct thing to say?
A. It's certainly not something that I would say, again, because I'm not willing to say that something is causal based

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on observational studies --
Q. I see.
A. -- observational data.
Q. And these guys have, it sounds like, a lower threshold for causation than you do, right?
A. I would say that, yeah, or they interpret that concept differently.
Q. And do you agree that it was reasonable to say that "the findings increased the probability that the association is causal"?
MR. MURDICA: Objection to the form.
THE WITNESS: Again, I think that is their interpretation.
My assessment based on the methodologic problems with the study is not consistent with that.
QUESTIONS BY MR. SNIDOW:
Q. But would you -- would you say that they're being quacks for saying that?
MR. MURDICA: Objection to the form.
THE WITNESS: Again, I don't

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know what a quack is, and I don't use that term. I find it somewhat derogatory.

I think that every epidemiologist is doing their best to interpret the evidence on a very important issue to the best of their ability using the training that they'd received and the way that they think about establishing causality.

QUESTIONS BY MR. SNIDOW:

Q. Right.

And you applied that analysis to this statement here when they say, "Increase the probability that the association was causal"?

MR. MURDICA: Objection to the form.

THE WITNESS: I believe that they were using their own training and their own interpretation to come up with that statement.

QUESTIONS BY MR. SNIDOW:

Q. Okay.

A. It's not something that I would

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say.

Q. Yeah. No, I get it.

And that's exactly what I mean. I know you disagree, but I'm asking if that's within the realm of reasonable debate?

MR. MURDICA: Objection to the form.

THE WITNESS: Yeah. I wouldn't call it debate, but I think it's interpretation, and people -- I would say that trained epidemiologists can interpret evidence differently.

QUESTIONS BY MR. SNIDOW:

Q. Including the evidence that they're describing here?

A. Including the evidence that they're describing here.

MR. MURDICA: Object to form.

QUESTIONS BY MR. SNIDOW:

Q. And then he goes on to say, "It's too simple and not justified to explain away the possibility of confounding" -- excuse me, I'll say it again. I screwed it up totally.

He goes on to say, "It is too

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simple and not justified to explain away the possibility of causality by mentioning confounding."

Do you see that?

A. I see that he says that, yes.

Q. And do you agree?

A. I do not.

Q. Okay. So you think it's fine to just mention confounding?

A. I'm not sure I understand your question. I think we must consider the possibility of confounding and look carefully at the possibility that confounding explains some or all of the association.

Q. Okay. But you need actual evidence of confounding before explaining away the possibility of causality, don't you?

A. You need evidence on the confounder that you're testing, and you need to be able to assess its impact on the results that you have reported, yes.

Q. And you need evidence both that it's associated with the outcome and that it's associated with the exposure, right?

A. Correct.

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Q. Correct.

Okay. Let's look at -- ah, same one. 1396, which is the next page.

All right. Do you see where it says, "The studies we are aware of covering the topic of fetal programming all find statistically significant results"?

A. I do.

Q. Okay. It says, "But that plays a limited role in our reading and interpretation of the data."

Right?

A. That's what they say.

Q. And you'd agree with that, right? That's what you've been telling me all morning?

MR. MURDICA: Objection to the form.

THE WITNESS: Not exactly sure what they're referring to there, if they're talking about mechanisms of action. I think -- I agree that I give it limited weight in my evaluation.

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QUESTIONS BY MR. SNIDOW:
Q. Yeah.
They go on to say, "More important is the methods and bias analyses that have been applied trying to make the association go away."
Right? They say that?
A. They say that, yes.
Q. And do you agree that researchers in this field have tried to make the association go away?
A. I think that's perhaps mischaracterizing it. I don't think we try to make an association go away. When we are doing an epidemiologic study, we evaluate the impact of potential confounders and biases on that measure of association to see whether it's credible.
Q. And do you see it says, "Comparison of exposure periods during and after" -- next page -- "pregnancy makes the case" -- "makes the case her own control could also help eliminate bias"?
A. So I know they're referring there to a negative control as we talked

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about before --
Q. Yeah.
A. -- using women prepregnancy and after pregnancy.
Q. Yeah.
A. And I would argue that that -- using that as a negative control has problems.
Q. Uh-huh.
A. Because we know that pregnancy changes a woman in all kinds of way, right, physical ways and her -- and perhaps could influence the pain that she's experiencing, her willingness to take a pain medication, and her necessity of taking acetaminophen as opposed to another medication that perhaps is no longer indicated during pregnancy.
Q. Yeah.
A. So using the woman as her own negative control I think has some problems.
Q. Okay. But I'm just asking, it's been done, right? They've done that.
8 refers to the Stergiakouli study. You know they did it in that one?
A. They did that in the

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Stergiakouli study. However, can I just point out that the Stergiakouli results that are reported in the main paper are the unadjusted results?
And when you look at the adjusted results in the supplementary table, they actually support the notion of unmeasured confounding.
Q. Okay. Did you write to Olsen and Liew to tell them that, that they got Stergiakouli wrong here?
MR. MURDICA: Objection to the form.
THE WITNESS: Again, as I've said before, that has not been the focus of the past six months of my life, but I am not ruling out the possibility that I would write a letter to the editor or to express my opinions about it at some point in time.
QUESTIONS BY MR. SNIDOW:
Q. Okay. I hope you do.
Do you see where it says "triangulation" here?

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A. I'm sorry, I lost the spot where you are.
Q. Do you see where it says "it's a term used to address a bias problem as approached from different angles"?
A. Yes, I see that.
Q. And you agree that's been employed here?
A. So I think what they're referring to here is looking at the cohort results and comparing it to the negative control exposure results, yes.
Q. Right.
So they've done that here?
A. They have done that.
Q. Okay.
A. Well, I guess that's what they're saying here.
Q. Yeah.
And then it says -- it quotes Arthur Conan Doyle. It says, "Once you eliminate the impossible, whatever remains, no matter how improbable, must be the truth."
A. I've seen that quote before.
Q. Yeah. It's in Bradford Hill,

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right?
A. It's in Bradford Hill, and it's in Baccarelli's report, yes.
Q. Yeah. Well, it's in Bradford Hill.
And then it says, "Such attempts have so far been unsuccessful."
Right?
A. That's what it says.
Q. And that's saying that they've tried to find evidence for other explanations other than causation and at least as of 2017, no luck, right?
A. I disagree with that statement. As I just pointed out in the Stergiakouli, for example, when they used a negative control exposure, both paternal and maternal prepregnancy use showed an increased risk of autism in the offspring, which supports the notion of familial or genetic confounding.
Q. Yeah, I know you disagree. I was actually just trying to get an interpretation of the sentence.
They're saying they've tried to eliminate other explanations, and those

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attempts have been unsuccessful, right?
MR. MURDICA: Objection to the form.
THE WITNESS: I see the sentence as it's written, and I'm saying I disagree with that statement.
QUESTIONS BY MR. SNIDOW:
Q. Okay.
A. Because I think that the attempts actually have demonstrated residual confounding.
Q. Okay. And that's Stergiakouli?
A. That's one example, yes.
Q. All right. Why don't you just give them all to me right now.
What else?
MR. MURDICA: Objection to the form.
THE WITNESS: I can't just rattle them off. I can look through the studies and describe where the negative control exposures or the maternal pre and post-pregnancy use have resulted in an increased risk in spite of the proposition that that

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would show no confounding, it shows there is confounding, and the same with paternity use.
QUESTIONS BY MR. SNIDOW:
Q. Could you do that on a break for me on as well?
MR. MURDICA: Objection to the form.
If you want her to do something --
THE WITNESS: I'm happy to look through my report and come up with them. I'm not going to try and do it from memory.
MR. SNIDOW: Thank you. That's all I'm asking.
THE WITNESS: And I can do it right now.
(Pinto-Martin Exhibit 610 marked for identification.)
QUESTIONS BY MR. SNIDOW:
Q. I'm going to -- I'm going to show you another study that I'm going to mark as Exhibit 610, which is the Gou paper.
All right. And you've read

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this one, right?
A. Yes, this is a meta-analysis.
Q. It is a meta-analysis.
If we turn to page 204.
Are you there?
A. I am there.
Q. It says, "These are validated, large prospective cohort studies and includes some analytical methods such as sibling-controlled analyses."
Right?
A. Correct.
Q. And this is before Gustavson, to be fair, right? So they don't cite it.
A. Right.
Q. But they do cite Brandlistuen, right?
A. Right.
Q. And that's a sibling-control study that showed a result even after doing the sibling controls?
A. That's correct, although Brandlistuen was based on a nondiagnostic outcome --
Q. Right.

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A. -- so...
Q. And you don't like those, right?
A. It's not that I don't like them.
MR. MURDICA: Objection.
THE WITNESS: I just don't think they are contributory to my opinion about the association between prenatal APAP exposure and the diagnosis of autism or ADHD.
QUESTIONS BY MR. SNIDOW:
Q. Yeah, and that's fair.
Then the Gou authors go on to say, "The most recent set of studies have consistently suggested a moderately increased risk from in utero acetaminophen exposure."
Right?
A. That's what they say.
Q. And they say, "These research findings lend weight to the hypothesis that the association is causal."
Right?
A. That's right. They're saying there's a hypothesis and the evidence is

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supporting the hypothesis of causality, but it's still a hypothesis.
Q. Right. No, I get it.
And I'm not asking you on the overall causation question, but do you think that's a reasonable thing for them to have said here?
MR. MURDICA: Objection to the form.
THE WITNESS: So, again, a meta-analysis is taking, you know, data that already exists. They don't -- they can't control how the data was collected and what the reliability of that information is. So given that caveat, that they're basing it on studies of that methodologic flaws and acknowledging that caveat, I think it's a reasonable statement.
QUESTIONS BY MR. SNIDOW:
Q. Okay. And then they say, "It's overly simplistic and not justifiable to explain away the possibilities of causality through confounding factors alone."

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Right?
MR. MURDICA: Objection to form.
THE WITNESS: I'm not sure I agree with that statement.
QUESTIONS BY MR. SNIDOW:
Q. Okay. Do you think it's reasonable for them to say it?
MR. MURDICA: Objection to the form.
THE WITNESS: I think if I wanted to answer that, I would want to read, you know, a couple of pages of this to really see where that's coming from. You're sort of pulling it out of context. I'm not sure exactly what they're trying to say there. So it's a little hard to react to a single statement like that.
QUESTIONS BY MR. SNIDOW:
Q. Okay. And then they call out confounding by indication in particular, right?
A. They do.
(Pinto-Martin Exhibit 611

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marked for identification.)
QUESTIONS BY MR. SNIDOW:
Q. All right. Let's look at J, which I'm going to mark as 611.
All right. And this one is Stergiakouli 2016?
A. It is.
Q. If you turn to page 967.
All right. And do you see at the bottom there it says, "These findings, when coupled with those from the previous discordant sibling-design study, suggests that the association between prenatal acetaminophen exposure and childhood behavioral problems is not explained by unmeasured familial factors linked to both acetaminophen use and childhood behavioral problems"?
A. I see that statement.
Q. Yeah.
A. And I think that that statement is actually a mischaracterization of the data. Because as I stated, if you pull the supplementary tables --
Q. Yeah.

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A. -- the effect in paternal use is actually greater than the effect in maternal prenatal use.

And this study had a whole set of commentaries that came following it because people actually accused her of mischaracterizing the data.

So I --

Q. Yeah.

A. -- I see that statement, but I think that it's not a fair summary of the data that she evaluated.

MR. MURDICA: Let me just add before you ask another question.

You have this tendency to comment while she's giving answers and to say, yeah, yeah, or other things, and I'm sure it's unintentional, but it's distracting, and I don't think it's the right thing to do.

So if you could try to stop it, I'd appreciate it.

MR. SNIDOW: Okay. It wasn't intentional.

MR. MURDICA: I said I don't

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think it's intentional. I think it's just a tick that you have.

MR. SNIDOW: Uh-huh, all right.

MR. MURDICA: Just try not to do it.

QUESTIONS BY MR. SNIDOW:

Q. All right. Are you ready, Doctor?

A. I am.

Q. Okay. What you're suggesting is that the authors of this study mischaracterized their own data?

A. I am.

Q. Okay. You see here where it says, "The findings are consistent with an intrauterine effect"?

A. I'm sorry, what page are you on?

Q. On 967, right at the bottom.

A. Right-hand column. Okay.

Q. You see it says, "The findings are consistent with an intrauterine effect"?

A. Yes, I see that.

Q. Do you think that's a reasonable thing to say?

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A. I do not think it's a reasonable thing to say because a negative control analysis is designed to address that question specifically: Is the effect an intrauterine effect? If so, you should not see an effect prepregnancy or post-pregnancy. You should not see an effect by paternal use.

And in her supplementary tables, she reports both.

(Pinto-Martin Exhibit 612 marked for identification.)

QUESTIONS BY MR. SNIDOW:

Q. Uh-huh. D is going to be marked as --

(Off the record discussion.)

MR. SNIDOW: And will you make sure that one is not highlighted.

THE WITNESS: It's highlighted.

MR. SNIDOW: It is? Trade me.

MR. MURDICA: He wants to trade.

THE WITNESS: Well, now I don't have one.

MR. SNIDOW: I know. I want you to have the real one.

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There you go.

THE WITNESS: Thank you.

MS. KO: J.J., do you happen to have an extra copy for me?

MR. SNIDOW: I do.

MS. KO: Thank you.

QUESTIONS BY MR. SNIDOW:

Q. All right. You reviewed this study when writing your report?

A. I did. This is a meta-analysis that I reviewed, yeah.

Q. If we could turn to page 1000.

Okay. Do you see it says, "The most consistent pattern of results was observed for the association between prenatal acetaminophen exposure and ADHD symptoms."

A. Yes, and I note the symptoms there.

Q. Yep.

And then it says, "Our findings are consistent with previous single-cohort studies conducted in the ALSPAC, DNBC and INMA cohorts."

A. And those also were studies that used ADHD symptoms, yes.

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Q. Yeah.
You see it says, "The association between prenatal acetaminophen use and ASC symptoms was consistently positive"?
A. I do see that.
Q. Okay. It says, "Associations between prenatal acetaminophen, ASC and ADHD symptoms were consistently positive for both boys and girls, albeit slightly stronger among boys."
Right?
A. I see that statement.
Q. And so these authors use the term "consistent" one, two, three, four -- four times in about three paragraphs?
A. That looks to be the case.
Q. And you disagree what the author is actually writing this paper, right?
A. I disagree with their overall evaluation of the body of evidence because, to my recollection, there's only one study in this meta-analysis that actually had ADHD as a diagnosis. And I think it's very important to think about the difference between results

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on a screening instrument, which are not diagnostic for ADHD, and the ADHD diagnosis itself.
There are many, many instruments that were used in this literature that have little to no bearing on the diagnosis of ADHD. And so I disagree with it because of that.
Q. Do you think that they're being bad epidemiologists for characterizing the literature as being consistent?
MR. MURDICA: Objection to the form.
THE WITNESS: I would never call someone a bad epidemiologist.
QUESTIONS BY MR. SNIDOW:
Q. Okay.
A. And I don't -- it's not the point of my disagreeing with their overall results. They can use consistent, if that's how they evaluate their results. That is not informative to my opinion about whether APAP exposure during pregnancy increases the risk of ADHD diagnosis.
Q. Well, let me ask you this.

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Let's say a series of results showed ten statistically significant negative results in a row. Okay?
.7, all the way down, statistically significant, right?
A. Insignificant or significant?
Q. Statistically significant.
A. .7?
Q. Yeah.
A. So a protective effect down the -- down the board.
Q. Yeah.
A. Okay.
Q. Do you think it would be unreasonable to characterize that -- those results as consistent in the positive direction?
MR. MURDICA: Objection -- objection to the form.
QUESTIONS BY MR. SNIDOW:
Q. Do you want me to draw?
A. So in the positive direction, so the result is .7, but you're claiming an increased risk?
You don't have to draw it.

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Q. Yeah. That's what I'm saying.
A. I think that would be a mischaracterization of the results.
Q. I agree.
And that's what I'm asking. Is that -- do you think that this is what they're doing here when they say consistent, or is it just a disagreement among epidemiologists about what counts?
A. As I said, I don't -- I don't disagree that they are interpreting their results as consistent. It does not inform my opinion as to whether there is a causal association between acetaminophen exposure and ADHD diagnosis because the results that they used in their meta-analysis were based primarily on screening instruments, which are not the same thing as a diagnosis.
As you know, screening instruments are designed to cast a wide net. So the sensitivity of those instruments is high in order to capture the risk pool, and that that group of individuals is then further evaluated for diagnosis where we establish a more specific outcome.

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Q. Okay.
A. So the two are very different in form.
Q. Do you see here they say, "The above-mentioned findings provide biological plausibility"?
A. I see that's what they say.
Q. Do you think that's a reasonable characterization of the evidence?
A. So I want to read the whole sentence. I don't believe that it establishes biological plausibility for a diagnosis of ADHD, which is what I was tasked with doing and what my review consists of.
Q. Yeah.
A. So, no. Again, picking one sentence out is -- sort of mischaracterizes their overall point. Because if you look at the beginning of the next paragraph, they say we need to interpret these results with caution --
Q. Sure.
A. -- because these are symptoms and not diagnoses.
Q. Okay.

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MR. MURDICA: Objection to the form.
QUESTIONS BY MR. SNIDOW:
Q. Do you agree that the results they describe above provide biological plausibility?
A. Not to a diagnosis of ADHD.
Q. So you disagree with the study authors again?
A. I do.
Q. How about coherence? Agree or disagree with the study authors?
A. Again, I am looking at this with respect to its influence on my opinion about prenatal APAP exposure and ADHD as an outcome, and I disagree with their characterization of their findings, and it does not inform my opinion.
Q. Okay. How about temporality? They say the temporality criterion has been satisfied.
Do you agree?
A. With respect to their analysis or in general?
Q. Uh-huh. With respect to their

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analysis.
A. Again, I think they're mischaracterizing the impact of APAP on these screening outcomes and inferring that because they found these effects in screening instruments, it establishes a risk for ADHD as a diagnosis.
Q. Well, it's not all screening instruments in this meta-analysis, right?
A. There's, I believe, one study.
Q. Yeah. Okay.
That uses diagnoses, right?
A. Yeah.
Q. All right. So just to be clear. And then they go on to say dose-response here.
And they think that the dose-response criteria in Bradford Hill has been satisfied?
A. And I disagree.
Q. All right. So you disagree with them -- the study authors themselves on --
A. Uh-huh.
Q. -- one, two, three, four, five,

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what, six of the Bradford Hill criteria?
A. I disagree with the summary of the data that these authors have presented --
Q. But do you --
A. -- in this form, and I think the supplementary tables inform my review and interpretation of this study.
Q. But you agree they are doing a Bradford Hill criteria -- Bradford Hill analysis here, right?
A. I never --
MR. MURDICA: Objection to the form.
THE WITNESS: They never state that, but those are the Bradford Hill criteria.
QUESTIONS BY MR. SNIDOW:
Q. Oh, really? What's footnote 42, do you think?
A. I'm just saying they don't state it in their paragraph.
Q. Well, but they cite to footnote 42.
A. Okay. So fine.
Q. Do you want to know what that

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is?
A. I mean, I said it's Bradford Hill criteria.
Q. Yeah. That's the Bradford Hill address? Yeah.
So in that paragraph, they're doing the Bradford Hill analysis, right?
A. They're doing a Bradford Hill analysis on data that is not complete --
Q. Okay.
A. -- because they have not included what the supplementary tables include.
Q. Okay.
A. And they are coming up with a summary of the findings based on incomplete presentation of the data.
Q. And that's fine.
MR. MURDICA: J.J., I'm going to ask you again nicely. I'm sure it's unintentional, but you keep doing it. You can't help yourself, and just please try.
QUESTIONS BY MR. SNIDOW:
Q. They say one, two, three, four,

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five -- six of the Bradford Hill criteria are satisfied?
A. I thought we just went through this, but that's what they say.
Q. Yeah. Okay. Thank you. You can put that one aside.
(Pinto-Martin Exhibit 613 marked for identification.)
QUESTIONS BY MR. SNIDOW:
Q. All right. Can I have L?
Are you familiar with the Briggs textbook?
A. I've seen it referred to in some of the expert reports. It's not a textbook I've ever looked at. It's not -- I would have no reason to. I'm not an obstetrician.
Q. Oh, is that what it's for? It's for obstetricians?
A. I believe so.
Q. All right. It says, "A Reference Guide to Fetal and Neonatal Risk."
Right?
A. My understanding is it's for clinicians, but, again, I've never seen it,

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so...
Q. All right. So this is designed for doctors who are dealing with pregnant women?
MR. MURDICA: Objection to the form.
THE WITNESS: I don't know what it was designed for. I wasn't part of its publication, but my understanding is that it's a reference for clinicians.
QUESTIONS BY MR. SNIDOW:
Q. And you see it's in its 12th edition?
A. I see that.
Q. So, yes, it's been around for a bit; is that right?
A. I would imagine. I don't know when the first publication was, but, yes, I would imagine it's been around for at least 12 years.
Q. All right. I'm going to mark it as 613.
A. Oh, boy, this one I really need my --

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Q. Yeah.
A. These give me a headache, that's the problem.
Yeah. That's really hard to read.
Q. You see here you've got a section on acetaminophen, right?
A. Uh-huh. Can this -- can this enlarge this little thing?
Q. Yeah.
A. That would be great, because this is really hard to read.
Q. Yeah, yeah, yeah.
MR. MURDICA: It's blurry on here too. I'm not sure that it's going to help it.
THE WITNESS: I think his copy is -- well --
QUESTIONS BY MR. SNIDOW:
Q. Is that better?
A. Did I mess it up?
Q. Good?
A. Does anyone know how this works? Oh, it's got to go -- we've got it. Thank you.

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Yeah, that's better. It's easier to read.

Do you want to look at this one, too? If you want --

Q. Are you ready?

A. Yeah.

Q. It says, "Acetaminophen is commonly used in all stages of pregnancy."

Right?

A. That's what it says.

Q. It says, "Although originally thought not to cause embryo-fetal harm, this assessment must change because of recent data."

Correct?

MR. MURDICA: Objection to the form.

THE WITNESS: There's what it says.

QUESTIONS BY MR. SNIDOW:

Q. And then it calls out ADHD in particular?

A. Although the risk is very low, use of the drug for seven -- several weeks or longer has been associated with -- (reading

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sotto voce).

It does. It does.

Q. And do you agree with the study authors?

A. As I've said, I do not believe there's credible epidemiologic evidence to support an increased risk of ADHD from prenatal APAP use.

Q. So you think that the Briggs textbook authors are wrong to be telling obstetricians that the assessment of APAP must change because of recent data?

A. I don't know anything about the Briggs textbook. I don't know who the authors are. I don't really know who the audience is, although I think it is clinicians, and I don't know what data they evaluated.

I don't know when this was written and why they decided to put this in there, so I really can't comment. It's not my area of expertise. I'm not willing to opine on why that's in there.

Q. Okay. You say you don't -- you don't make causal determinations on the basis

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of observational data; is that right?

A. That's right.

Q. All right. Do you make causal determinations on the basis of randomized controlled trials?

A. I don't know that I've ever made a causal determination on the basis of an RCT. I have been involved with some RCTs. They certainly rule out many of the problems of confounding and bias that a observational study contains.

So I would say I would be more likely to accept evidence from an RCT than I would from an observational study with respect to establishing a causal association.

Q. Well, isn't that how the FDA determined whether drugs work, because they do RCT?

MR. MURDICA: Objection to the form.

THE WITNESS: I'm have no idea hat the FDA does. I'm not an FDA employee. I don't know what kinds of studies they do or how they evaluate their evidence.

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QUESTIONS BY MR. SNIDOW:

Q. You really don't know before approving a drug the FDA requires a randomized control trial?

MR. MURDICA: Objection to form.

THE WITNESS: I know that there are a series of steps you have to go through to approve a drug, but it's not something that I've ever studied or know about.

QUESTIONS BY MR. SNIDOW:

Q. Okay. Do you think that an RCT would pretty definitively answer the question of whether acetaminophen use in utero causes autism?

A. Well, it's a hypothetical that's impossible to do, so I've never really given it consideration. You can't randomly assign women to receive a medication that at this point has some suggestion of harm.

Q. Right.

Yeah. So that's kind of what I was getting at. You think it would be unethical, right?

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MR. MURDICA: Objection to the form.
THE WITNESS: We do not allow randomized clinical trials, except at the moment of what we call equipoise, where there is not sufficient evidence on one side or the other.
It's very hard to establish that point in time, and I think we're past that now because there are studies suggesting a risk.
And so, first of all, which -- what women would enroll in a study like that? And it would be unethical.
QUESTIONS BY MR. SNIDOW:
Q. And suggesting the risk of what?
MR. MURDICA: Objection to the form.
THE WITNESS: I'm sorry? I just lost you there.
QUESTIONS BY MR. SNIDOW:
Q. You said there are -- you can't do it at this point because there's studies suggesting the risk. Suggesting the risk of

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what?
A. So there's studies that report an elevated risk of ASD, ADHD and some findings on screening instruments that are very flawed but nonetheless have been published and have been picked up by the media.
And so that information is out there, and the public has digested it and --
Q. And because of that, you can't do a clinical trial anymore, right?
MR. MURDICA: Objection to the form.
THE WITNESS: Because of that and because in general we don't allow pregnant women to enroll in clinical trials because of the vulnerability of the fetus.
QUESTIONS BY MR. SNIDOW:
Q. Right.
But put just the general pregnancy point aside. You actually don't think that there's a causal association between APAP and autism or ADHD, right?
A. That's correct.

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Q. And you're 100 percent certain of that, right?
A. As I said, I am certain based on the body of literature that I've reviewed that no evidence for a causal association exists for ASD or ADHD.
Q. That's a little different, though.
Are you certain that it doesn't cause it?
A. As I said, all I can be certain on is what I've reviewed and evaluated, and I've reviewed and evaluated the studies, and my conclusion on the basis of that review and evaluation is that there's not credible evidence of a causal association for either of those outcomes.
Q. So why would it be unethical to do the RCT?
MR. MURDICA: Objection to the form.
THE WITNESS: It's unethical to do RCTs in pregnant women.
QUESTIONS BY MR. SNIDOW:
Q. Put that one aside.

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A. I can't put that one aside. It's --
Q. It's not the one you told me first. You said it would be unethical because of what we know now on risk.
MR. MURDICA: And objection to the form. And you -- please stop. You really got to stop interrupting the witness.
QUESTIONS BY MR. SNIDOW:
Q. Go ahead.
Why -- why would the risk of APAP, which you think is entirely the result of confounding and bias -- why would that preclude you from doing an RCT on ethical grounds?
MR. MURDICA: Objection to the form.
THE WITNESS: So I think it would be unethical to ask a woman to enroll in a study where she has heard on media or law websites that this substance might put her baby at risk.
I think just the suggestion of an association is enough to make a

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woman worry, and I think it would be unethical to subject a woman to that kind of -- of worry and anxiety. So it's unethical from that reason.

QUESTIONS BY MR. SNIDOW:

Q. Can you point me to any publication or authority that says it's unethical to do a clinical trial based on what's been reported in the press rather than the science?

MR. MURDICA: Objection to the form.

THE WITNESS: I can point to a textbook definition of equipoise, which I think speaks to this exact issue, that a clinical trial can be launched when we are at a point where nobody really knows anything about the risk, and you can legitimately enroll people and expose them to something because we have no evidence to suggest that that exposure might increase the risk.

And as I've said, there are reported elevated risk estimates from

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these studies that have been captured and publicized, and so we are not at the moment of equipoise.

QUESTIONS BY MR. SNIDOW:

Q. We're not at the moment of equipoise?

A. We are not at the moment of equipoise.

MR. SNIDOW: Okay. Jim, can we take a quick break?

MR. MURDICA: We're taking lunch in eight minutes.

MR. SNIDOW: Okay. Perfect.

QUESTIONS BY MR. SNIDOW:

Q. All right. Can you go to page 36 of your report?

A. Yes.

Q. And there you report a set of results for autism and prenatal APAP use?

A. Correct.

Q. You chose these again?

A. I did.

Q. And you report, I think you say, five of them?

A. That's right.

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Q. All right.

A. Yeah.

Q. Yeah.

A. Liew, Ji, Ji, Hornig and Saunders.

Q. Okay. And you told me before that Liew 2016 is the strongest, the best?

A. So Liew 2016 is based on the largest sample with, I would say, the most accurate, although very imperfect, measure of exposure. So among this group, I would describe it as the methodologically strongest.

Q. Yeah. Remember you said -- I asked what are the better-designed studies, you said Liew 2016, right?

A. As I said, among the five studies, I think this one has strengths over the others. It still has many problems, but it has strengths over the others.

Q. Okay. So the result for ASD there was 1.19?

A. That's correct. The overall result for ASD was 1.19.

Q. And that's statistically

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significant?

A. It is in the report, yes.

Q. All right. And you said in your report the better-designed studies don't show an association, right?

MR. MURDICA: Objection to the form.

QUESTIONS BY MR. SNIDOW:

Q. On page 5. Remember that?

A. I'm reminding myself of my exact phrase, but, yes, that does sound familiar.

Q. Okay. And Liew, that's the better-designed study you're referring to?

A. Among the five that report on ASD outcome, this one is based on the best-designed study, yes.

Q. Okay. And would you mind looking at the table real quick and just telling me if my forest plot here -- if you see any obvious errors?

MR. MURDICA: Objection to the form and the use of this demonstrative.

MR. SNIDOW: In most

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litigations, you guys like the forest plot.

THE WITNESS: It looks to be an accurate representation of what I had in the table.

QUESTIONS BY MR. SNIDOW:

Q. Okay. All right. Do you agree that all the results except for this one here have a point estimate above 1.0?

A. That is what is reported by the authors. That is what is reflected in your forest plot here. And again, it is one measure of -- one aspect of my interpretation of these data, and I have to always characterize it in the context of the underlying data on exposure, which is exceedingly weak.

So a point estimate that's above 1 based on data that I think is highly flawed is not the same thing as a point estimate of above 1 on data that is solid and reliable and valid.

Q. Yeah, and I get it. I just -- just to be clear, though, for what that means, the point estimate above 1 means in

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all these studies except for this subgroup, the woman who was exposed to APAP, or in this case more APAP, had a higher rate of having a child with ASD, right?

MR. MURDICA: Objection to the form.

THE WITNESS: That is what the study authors have reported. However, I don't think that that's a fair characterization of the data because the underlying exposure information is so flimsy that it doesn't hold up in my mind in terms of characterizing an increased risk.

QUESTIONS BY MR. SNIDOW:

Q. Okay. But it's an accurate representation of the results, right?

A. The point results -- the point estimates are above 1 and statistically significant, and those have to be evaluated in the context of the -- of the quality of the underlying data.

MR. MURDICA: Objection to the form.

MR. SNIDOW: All right.

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Lunchtime?

MR. MURDICA: Sure.

VIDEOGRAPHER: The time is 12:19 p.m., and we are off the record.

(Off the record at 12:19 p.m.)

VIDEOGRAPHER: The time is 12:54 p.m., and we're on the record.

QUESTIONS BY MR. SNIDOW:

Q. Okay. Dr. Pinto-Martin, when you were on break, did you -- did you find that study you were telling me about where it showed that pre or post-pregnancy use was associated with an autism diagnosis in the child?

MR. MURDICA: Objection to form.

You know we just had a break for lunch. That's what Dr. Pinto-Martin did, was she ate lunch.

QUESTIONS BY MR. SNIDOW:

Q. Okay. So sorry, did you find that article?

A. I didn't have time. I barely had time -- I didn't even time to finish my

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lunch.

So I'm sorry, I did not have time to do that.

Q. Would you mind looking on the next break?

MR. MURDICA: Objection to form.

Just stop asking. Okay? You don't get to tell the witness what to do.

MR. SNIDOW: Well, here's the thing. Here's the thing. I don't think it exists, and I really want to be sure of that.

MR. MURDICA: We don't care about your opinion. Just ask questions.

QUESTIONS BY MR. SNIDOW:

Q. So will you next time -- I'm going to ask you every break, because it's not fair. Okay?

You've got to tell me if these exist or don't exist, so I want you to look --

MR. MURDICA: Please conduct

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yourself appropriately, Mr. Snidow. That's not --

QUESTIONS BY MR. SNIDOW:

Q. Okay. Could -- I'm going to show you this demonstrative.

Do you remember the secondhand smoke data we were looking at?

A. I remember that, yes.

Q. And you remember the risk ratios were all between about -- well, a little bit negative and a maximum of 1.3 or so?

A. Are we talking about the sibling -- I mean, the spouse or the child?

Q. Actually, all of them.

A. Okay.

Q. Sure.

A. Yeah, I would like to refresh, but, yes, that sounds about right.

Q. All right. And I'm not saying exactly, but this is approximately what that association looks like; that you get a third more than in the no secondhand smoke one?

MR. MURDICA: Object to the form and the use of the demonstrative

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you created.

THE WITNESS: I mean, I think we have the point estimates in the report, so I don't know why we need to see a graphic demonstration of it. I don't -- I don't really feel like that adds anything, but --

QUESTIONS BY MR. SNIDOW:

Q. Yeah. I'm just -- is it an accurate graphic demonstration, though?

This is what a risk ratio of 1.3 in the secondhand smoke literature, that's what it looks like.

A. I mean, if you were -- yeah --

MR. MURDICA: Objection to the form.

THE WITNESS: Again, it just seems a strange way to take an actual, established risk. This is more of a teaching method to show how we might derive it, but it's not wrong.

QUESTIONS BY MR. SNIDOW:

Q. Okay. Thank you.

Has there ever been a randomized controlled trial on the

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relationship between active smoking and lung cancer?

A. I do not believe that a randomized controlled trial would have ever been authorized because of ethical considerations.

Q. So it wasn't an equipoise, right? At least after the '50s or so?

A. Right. As soon as we had established that there was potential for increased risk, we are beyond the point of equipoise.

Q. Yeah.

Do you agree that in the middle of the 20th century, '50s or so, there were many epidemiologists who argued that the relationship between smoking and lung cancer was due to confounding?

A. I was not reviewing epidemiology studies on smoking and lung cancer in the '50s.

Q. Uh-huh.

A. I was a child. So I can't really respond to that.

Q. Okay. Do you agree, though,

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it's always theoretically possible to say that a result might be due to unmeasured confounding?

MR. MURDICA: Objection to form.

THE WITNESS: Do I agree that it's always theoretically possible?

I mean, unmeasured confounding is a fact of life in observational studies, and we always assess for the risk of that in our analytic strategies. Or at least I do, and I think most reasonable epidemiologists do.

So I think that's how I would describe it, is when you're doing your analysis, you look at the putative confounders and assess for them if you have data on them.

QUESTIONS BY MR. SNIDOW:

Q. Right.

That's what I'm saying. It's always possible that you missed something.

MR. MURDICA: Objection to form.

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QUESTIONS BY MR. SNIDOW:
Q. Right?
A. It's always possible that you missed something. I mean, that's a very general statement.
Q. Okay. Do you remember this?
A. I remember this, yeah.
Q. No matter how good your study is, it's always possible that there's some confounder out there that's actually driving the results.
Is that true?
MR. MURDICA: Objection to form.
THE WITNESS: Absolutely true.
QUESTIONS BY MR. SNIDOW:
Q. Absolutely true. Okay.
And same thing for residual confounding, right? Even if you've controlled for something explicitly, it's possible that your data sucked, right?
MR. MURDICA: Objection to form.
THE WITNESS: That's one interpretation.

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QUESTIONS BY MR. SNIDOW:
Q. And in that situation, it's theoretically possible that there's residual confounding?
A. Residual confounding is always a possibility.
Q. And that's my question.
No matter how good your study is, best study in the world, outside of the RCT context, there's always going to be the possibility for residual and unmeasured confounding, right?
A. Which is why I talk about the challenges of observational studies.
Q. No, I agree.
A. Epidemiology.
Q. Do you agree with me, though, always possible, every study, no matter how good?
MR. MURDICA: Objection to form.
THE WITNESS: That's a very firm, broad statement. I don't know. Maybe there's -- maybe there is a perfect observational study that could

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be designed that was free of bias and confounding. I haven't seen it, but I couldn't say that it would never be possible.
QUESTIONS BY MR. SNIDOW:
Q. Have you ever seen one like that?
A. I've never seen one.
Q. No.
Is that a no, you've never seen one like that?
MR. MURDICA: Objection to form.
THE WITNESS: I've never seen a study like that, but I'm saying --
QUESTIONS BY MR. SNIDOW:
Q. Sure.
A. Maybe someone could do it.
MR. MURDICA: You're doing it again. You just did "okay" and "sure" there, and I know you're saying it's not intentional, I don't think it is, but if there's any way to stop it, it's very distracting, and it interrupts the witness.

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(Pinto-Martin Exhibit 617 marked for identification.)
QUESTIONS BY MR. SNIDOW:
Q. I'm going to show you a document that I'm marking 617.
MR. MURDICA: Well, are you going to acknowledge that you're going to try to fix that or not?
MR. SNIDOW: No, I'm not.
MR. WATTS: Don't talk to him. Keep asking questions. Come on.
MR. SNIDOW: Here's one for you.
Let's just move on. Let's just move on.
MR. MURDICA: You keep talking in the middle of her answers.
MR. SNIDOW: Ladies, please, you're both pretty. Let's move on. Okay?
MR. MURDICA: I don't even know what that means. That seems wildly inappropriate to say to a female witness. I don't know --
MR. SNIDOW: I wasn't --

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MR. MURDICA: -- what your problem is --
THE WITNESS: I'm really offended by that.
MR. SNIDOW: I wasn't talking to the witness.
THE WITNESS: I'm sure you weren't, but it's still an offensive comment, so --
MR. SNIDOW: I was talking to Mr. Watts.
MR. MURDICA: You need --
THE WITNESS: It's still an offensive comment, so --
MR. MURDICA: You need to get it under control real quick.
MR. SNIDOW: Okay.
THE WITNESS: I find that offensive.
QUESTIONS BY MR. SNIDOW:
Q. You see this Smoking and Health from the Surgeon General?
A. I do.
Q. This is the report that was used to establish likelihood of causation for

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tobacco?
MR. MURDICA: Objection to the form.
THE WITNESS: I don't know how this report was used, but if I have a chance to read it, I can look to see who called for it and to whom it went and what was done with the data.
But I don't know looking at it right now.
QUESTIONS BY MR. SNIDOW:
Q. You really haven't seen the Surgeon General report on smoking and health?
MR. MURDICA: Objection to the form.
THE WITNESS: I have not read this report.
QUESTIONS BY MR. SNIDOW:
Q. Okay. Well, let's look at page 593.
Oh, I'm sorry, 190.
A. Okay.
Q. All right. Do you see where it says "Constitutional hypothesis"?
A. I do.

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Q. And it says, "Thus far in the evaluation, the committee has considered whether the available data are consistent with the hypothesis that smoking causes cancer of the lung."
Do you see that?
A. That is the first sentence of that paragraph.
Q. Then it says, "The analysis must consider with equal attention the alternative hypothesis that both the smoking of cigarettes and cancer of the lung have a common cause which determines both that an individual shall become a smoker and also that he shall be predisposed to lung cancer."
Right?
A. That's correct.
Q. And that's describing confounding, right?
A. That's describing confounding.
Q. And what that's suggesting is, oh, well, maybe there's something out there that's associated both with smoking and with lung cancer, and we just haven't found it yet.

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Right?
A. That is what that's suggesting, I would agree.
Q. And that argument is, though, the one you're making here, right; that there's a confounder, mainly genetics and indication, that's associated both with prenatal APAP use and autism.
True?
MR. MURDICA: Objection to the form.
THE WITNESS: So the difference, I would say, is that I think we have evidence that both genetics and indication of use act as potential confounders in that relationship.
QUESTIONS BY MR. SNIDOW:
Q. Yeah. I'm obviously not saying they were right. I'm just saying the form of the argument is the same one that you're making, right?
A. Uh-huh.
Q. Yeah.
And, actually, it's a little

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more specific, because if you look down a little bit farther down the page, it says, "Fisher has been foremost in calling attention to the possibility that cancer of the lung and the habit of smoking may be due to a common genotype."

Is that right?

A. I see that sentence.

Q. Do you know who Ronald Fisher was?

A. I imagine --

MR. MURDICA: Objection to the form.

THE WITNESS: -- it's Fisher, the statistician, but I have no idea based on this.

QUESTIONS BY MR. SNIDOW:

Q. It is.

And who is Fisher, the statistician?

A. He is a famous statistician who developed the Fisher's exact test.

Q. Yes.

And the F-test is named for him?

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A. I believe that's correct.

Q. The Student t-test that he was -- he developed it or helped to?

A. I don't know exactly what he did or didn't do, but I know that he's a statistician that is often cited.

Q. But possibly the most important statistician of the 20th century; is that right?

MR. MURDICA: Objection to form.

THE WITNESS: I can't characterize him that way. I know that I studied his textbook when I was in graduate school.

QUESTIONS BY MR. SNIDOW:

Q. He came up with the concept of the null hypothesis?

MR. MURDICA: Objection. Form.

THE WITNESS: I believe that's true.

QUESTIONS BY MR. SNIDOW:

Q. You said you believe that's true?

A. Uh-huh.

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Q. Okay. That's a pretty good contribution to the literature, don't you think?

MR. MURDICA: Objection to form.

THE WITNESS: I agree. He's an important statistician.

QUESTIONS BY MR. SNIDOW:

Q. And he said that "The habit of smoking may be due to a common genotype with lung cancer," right?

A. That's what that says.

Q. "Selection of smokers then would automatically provide a population in which pulmonary cancer would appear on the basic of" -- "basis of genetic susceptibility."

Right?

A. That's a hypothesis that he's putting forth, if that confounder is there.

Q. And that is, if I understand correctly, exactly the same argument that you're making with respect to prenatal APAP use, autism and ADHD, right?

MR. MURDICA: Objection to

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form.

THE WITNESS: Again, I'm trying to get a sense, you know, of the whole -- of the whole argument here because just pulling the one line out is a little hard for me to react to.

QUESTIONS BY MR. SNIDOW:

Q. Yeah, go ahead and read.

A. Okay. I think I -- I think that his illustration of the potential role of genetic confounding is similar to what I'm arguing in my example here.

Q. Yeah.

A. Well, your example here because I made it generic, and you've now made it specific to APAP and autism.

Q. Yeah, that was okay.

Right?

MR. MURDICA: Objection to form.

QUESTIONS BY MR. SNIDOW:

Q. Did you mind that I made the confounding diagram?

MR. MURDICA: Objection to form.

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THE WITNESS: I think it's irrelevant whether I find it --
QUESTIONS BY MR. SNIDOW:
Q. Well, sorry. It does describe what you think is going on here, right?
MR. MURDICA: Objection to form.
THE WITNESS: It does describe what I have proposed.
QUESTIONS BY MR. SNIDOW:
Q. All right. And let's look at what evidence Fisher relied on for his genetic confounding theory.
He points to studies on monozygotic pairs of twins; is that right?
MR. MURDICA: Objection to form.
THE WITNESS: He does point to the difference between monozygotic twin pairs and dizygotic twin pairs in terms of smoking.
QUESTIONS BY MR. SNIDOW:
Q. And that is exactly the same kind of evidence that you point to to show that autism is genetic, right?

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MR. MURDICA: Objection to the form.
THE WITNESS: The basis of the heritability estimate for autism is the concordance rate for monozygotic twins and dizygotic twins, yes.
QUESTIONS BY MR. SNIDOW:
Q. And that's Fisher's statement for saying that it might be genetic confounding in smoking and lung cancer; is that true?
MR. MURDICA: Objection to form.
THE WITNESS: I believe that that's what he's saying in this paragraph, not having read the entire report, pulling that out.
QUESTIONS BY MR. SNIDOW:
Q. He goes on to say that "The data on smoking habits of identical and fraternal twins raised apart are compatible with that hypothesis."
Do you see that?
A. Again, this is very hard for me to do, to be reading sentence by sentence and

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not understanding the whole context. I'd sort of like to take a minute and read the whole couple of paragraphs and maybe a couple of pages to understand exactly what his argument is and what the flow of his argument might be.
Q. Okay.
A. Because you're taking one sentence at a time, and it's hard to react to them --
MR. MURDICA: You can. You're allowed --
THE WITNESS: -- in isolation.
MR. MURDICA: You're allowed to.
THE WITNESS: Yeah.
QUESTIONS BY MR. SNIDOW:
Q. Yeah. You can look.
A. I'll do it this way.
Okay.
Q. All right. Are you ready?
A. Well, I can stop --
MR. MURDICA: You let him -- you can tell him when you're ready. You take as much time as you need.

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THE WITNESS: I mean, I can read -- read on.
QUESTIONS BY MR. SNIDOW:
Q. No.
MR. MURDICA: Well --
THE WITNESS: Because it's all -- I don't know what you're going to ask me about.
QUESTIONS BY MR. SNIDOW:
Q. Right. So let me --
A. But I'd like to understand the whole --
Q. So let me -- let me try to walk you through it.
Richard {sic} Fisher also pointed out that cigarette smokers were different in certain ways than people who didn't smoke cigarettes.
Right? Did you see that there?
A. He does talk about the differences, yes.
Q. And you think that women who take APAP while pregnant are different than women who do not take APAP in certain ways, right?

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MR. MURDICA: Objection. Form.
THE WITNESS: I think there's evidence to suggest that women who take APAP during pregnancy are more prone to depression and to anxiety and to comorbid symptomatology that means that they're willing to continue to take medication during pregnancy or they need to continue to take medication during pregnancy.
QUESTIONS BY MR. SNIDOW:
Q. Including neuroticism.
Is that right?
MR. MURDICA: Objection. Form.
THE WITNESS: What do you mean "including neuroticism"?
QUESTIONS BY MR. SNIDOW:
Q. Do you think that women who take APAP are more likely to be neurotic than women who don't?
A. So there is a study that evaluated the trait of neuroticism and supports the idea that women who have more neurotic traits are more likely to take APAP during pregnancy.

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Q. If we look up here, it says, "Cigarette smokers have been described as consuming more alcohol, drinking more, being more neurotic, engaging more often in athletics and being more likely to have at least one parent with hypertension or coronary diease."
Right?
A. Okay. So now you're jumping up to a paragraph that I haven't even looked at yet, so --
Q. Right. Take a look. Take a look.
A. Can -- can I just --
Q. I had said you can have as long as you like. So take a look.
A. Okay. I want to read the whole thing. Genetic considerations.
When was this written? It's sort of making me laugh because some of the terms that are used.
Q. Yeah, no. It is -- it is dated.
A. Masculinity.
Q. Yeah. That's -- they thought

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that might have been one of the confounders, too.
A. Uh-huh.
Q. Hold on, and I'll tell you.
1964.
A. Okay. Okay. I mean, I think I've got the flavor of it.
Q. Okay. You got -- you got the gist of it?
A. Yeah.
Q. All right. He's suggesting that there's confounding because cigarette smokers are different in certain ways than non-cigarette smokers, right?
A. Uh-huh.
Q. And some of the ways are the same ones that you point to here, right, alcohol?
A. Uh-huh.
Q. Neuroticism?
A. Again, there's a study that suggests that, yeah.
Q. And family history, right?
A. Right, which would be, I guess, genetics --

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Q. Yeah.
A. -- as explained through family history, yeah.
Q. Okay. And just to be clear, you think that this was very wrong for him to suggest at the time, right?
MR. MURDICA: Objection. Form.
THE WITNESS: I never said that I thought it was very wrong for him to suggest at the time. I didn't know he suggested it at the time. I'm reading this for the first time.
QUESTIONS BY MR. SNIDOW:
Q. Okay. Do you think that was wrong of him to suggest at the time?
A. No. I don't think it was wrong of him to suggest at the time. It was a hypothesis that was put forth to test with data.
Q. Yeah.
So you think it was fine for Fisher in 1964 to suggest that maybe the relationship between smoking and lung cancer was the result of confounding?
MR. MURDICA: Objection to

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form.
THE WITNESS: I'm sorry, can you repeat the question?
QUESTIONS BY MR. SNIDOW:
Q. Yeah.
You think it was fine for Fisher in 1964 to suggest that the relationship between smoking and lung cancer was possibly due to confounding?
MR. MURDICA: Objection to form.
THE WITNESS: I think it was a reasonable hypothesis that he was putting forth to see if it could be tested.
QUESTIONS BY MR. SNIDOW:
Q. Okay. Do you know what the risk ratios for smoking and lung cancer are?
MR. MURDICA: Objection to form.
THE WITNESS: Not off the top of my head, but I imagine they're quite high.
QUESTIONS BY MR. SNIDOW:
Q. Double digits?

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MR. MURDICA: Objection to form.
THE WITNESS: Again, I don't know without looking at a specific study.
QUESTIONS BY MR. SNIDOW:
Q. Okay. Do you think it's -- well, never mind. That's fine.
Are you aware that one of the pieces of evidence that the Surgeon General considered pretty compelling was the fact that lung cancer and cigarettes had gone up in the same fashion over the decades preceding the 1960s?
MR. MURDICA: Objection to form.
You can answer.
THE WITNESS: I have no idea what the Surgeon General considered in terms of the overall evidence. That is ecological evidence.
And as we know, ecological evidence is very easily explained by other factors, and that's certainly true in the acetaminophen and

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neurodevelopmental disorder story as well.
QUESTIONS BY MR. SNIDOW:
Q. Can you look at page 179 of this?
You see direct measure of the association?
A. Uh-huh.
Q. Do you see that there were seven prospective studies at this time on smoking and lung cancer?
A. "Seven prospective studies consider the occurrence or lack of occurrence of lung cancer among smokers and nonsmokers."
Yes, I see that.
Q. Do you think that's a consistent association?
MR. MURDICA: Objection to form.
THE WITNESS: Again, I don't have the studies in front of me. If I had time to review them and look at the data behind those -- behind that statement, I'd be happy to give an opinion.

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QUESTIONS BY MR. SNIDOW:
Q. Okay. Do you see here it says, "Others believe that the lung cancer rise is spurious and can be attributed either to improvements in diagnosis and reporting"?
A. I do see that statement.
Q. Okay. And --
MR. MURDICA: You didn't read it all in there.
MR. SNIDOW: Oh, I'm sorry.
MR. MURDICA: You didn't complete the sentence.
QUESTIONS BY MR. SNIDOW:
Q. "Or to the aging of the population."
Do you see that?
A. I see that statement, yes.
Q. And so what the -- what the smoker skeptics here are suggesting is that there's a difference between the prevalence and the incidence rate for lung cancer, right?
MR. MURDICA: Objection to form.
THE WITNESS: Again, I think

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you're inferring something that they are not stating here, but I understand why you say that. You know, prevalence and incidence are different, as we talked about before.

QUESTIONS BY MR. SNIDOW:

Q. Well, they're saying the lung cancer rise is spurious, true?

MR. MURDICA: Objection to form.

THE WITNESS: They're saying that some believe that the lung cancer rise is spurious and might be a diagnostic reporting issue, ascertainment issue.

QUESTIONS BY MR. SNIDOW:

Q. Yeah.

And that's what you think is going on here with autism?

MR. MURDICA: Objection to form.

THE WITNESS: So I think that the data supporting the increased prevalence of autism, which I am very familiar with because I was part of

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the team that has been collecting that data for the CDC, uses a methodology that relies on medical records alone. There's no in-person evaluation of children.

We've been doing it now for about ten years or more. And the methodology is, I would say now, somewhat biased by the fact that we continue to do it.

And I'd be happy to talk about the specifics of that bias, but I believe there is some perhaps overascertainment or overcalling of the presence.

That being said, that's only one reason why the prevalence might be increasing over time. We know that the diagnostic criteria has changed, and at least prior to the most recent change to DSM-5, the umbrella was larger, and it was easier to be labeled with autism spectrum disorder than it had been in the past.

Furthermore, the awareness of

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autism and the likelihood of early detection has been dramatically changed over the past 10 to 15 years because of public awareness.

So all of those things are going to contribute to an inflated prevalence estimate, and none of them address the issue of whether there's actually an increased incidence.

QUESTIONS BY MR. SNIDOW:

Q. So is that a, yeah, you think that the rise in autism is a spurious -- a spurious one?

MR. MURDICA: Objection to form.

THE WITNESS: I'm not saying that the -- I'm saying that there are methodologic reasons that contribute to the increased prevalence, and we need to acknowledge those and not assume that it's due to an actual increase in the risk of acquiring the disease --

QUESTIONS BY MR. SNIDOW:

Q. Okay.

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A. -- which would be the incidence.

Q. Can you go to 27 for a second?

A. (Witness complies.)

Q. Actually, I'll do it with a different statement. Okay.

(Pinto-Martin Exhibit 614 marked for identification.)

QUESTIONS BY MR. SNIDOW:

Q. I'm going to show you an exhibit I'm going to mark as GGG, and that will be -- thanks -- mark as 614.

A. Thank you.

Q. Okay. Do you see this is a letter to the editor in Nature in 1958?

A. I do.

Q. Nature is a pretty good journal, right?

MR. MURDICA: Objection to the form.

THE WITNESS: I have no idea what Nature in 1958 was like.

QUESTIONS BY MR. SNIDOW:

Q. Okay. Pretty good journal today?

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A. Nature -- Nature today has a good reputation.
Q. And do you see this is from Ronald Fisher?
A. Sure enough.
Q. Part of genetics at Cambridge, right?
A. Uh-huh.
Q. And he's talking about cancer and smoking, right?
A. Uh-huh.
Q. And he says, "Such results suggest that an error has been made of an old kind in arguing from correlation to causation," right?
A. I'm sorry, I've lost where you are.
MR. MURDICA: Where are you?
QUESTIONS BY MR. SNIDOW:
Q. Second paragraph.
A. Such results -- okay. Again, I'd like to read this whole thing. I'm fascinated by this actually, being a historic epidemiologist.
But can I read the whole thing?

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Q. Uh-huh.
A. Okay.
MR. MURDICA: I think I showed up to the wrong deposition. I was planning to do one on acetaminophen, and we're --
THE WITNESS: Curious relation.
MR. MURDICA: -- it's on smoking.
THE WITNESS: This is great. I'm going to use it in my teaching. It's good.
He was a good writer. You got to give him that.
QUESTIONS BY MR. SNIDOW:
Q. Uh-huh.
A. This is great.
Okay.
Q. I'm glad you think so.
Okay. You see where it says, "Such results suggest that an error has been made of an old kind arguing from correlation to causation"?
A. I do.
Q. And that's the error that you

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think -- you think the plaintiff experts are making here, right?
MR. MURDICA: Objection to the form.
THE WITNESS: So I would say that's an oversimplification of the error that I believe has been made. I think it's certainly part of it, but...
QUESTIONS BY MR. SNIDOW:
Q. Okay. Then he repeats his genetic confounding argument, right?
A. Uh-huh.
Q. Then he goes on to say, "Unfortunately, considerable propaganda is now being developed to convince the public that cigarette smoking is dangerous."
Right?
A. That's what he says.
Q. And you agree that that propaganda which he said was dangerous to the public ultimately turned out to be 100 percent correct, right?
MR. MURDICA: Objection to the form.

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THE WITNESS: So I believe that that was a statement that he made at the time that he believed was true, and I believe later the evidence was counter -- ran counter to that.
QUESTIONS BY MR. SNIDOW:
Q. And do you think that the people who were promoting evidence in favor of the link between tobacco and cigarette smoking were wrong to promote it, even before the link was 100 percent definitive?
MR. MURDICA: Objection to form.
THE WITNESS: That's a hard question to answer because I don't know what the weight of the evidence back was when people were putting forth their belief that it was dangerous.
So it's really sort of impossible for me to say whether it was right or wrong. I imagine they were doing it with the best intention, but I really have no way of knowing. It was a long time ago.

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QUESTIONS BY MR. SNIDOW:
Q. Well, I'm talking about the ones who are saying that tobacco does cause lung cancer. Those guys were definitely right to promote that view, right?
MR. MURDICA: Objection to form.
THE WITNESS: Again, without knowledge of what the state of the evidence was at the time that they were promote -- promoting that view, I would not be willing to comment.
QUESTIONS BY MR. SNIDOW:
Q. Okay. So you can't give me a clean answer on whether the people in the 1950s and early 1960s who said, "Yes, tobacco does cause lung cancer," whether they were right to promote that view?
MR. MURDICA: Objection to form.
THE WITNESS: Again, I was not around to see the data that was being relied upon to make statements about that, so I would not be willing to give an opinion on whether they were

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right or wrong.
QUESTIONS BY MR. SNIDOW:
Q. Isn't it generally considered the biggest achievement in epidemiology what they did?
MR. MURDICA: Objection to form.
THE WITNESS: I don't have an opinion on that. I've never --
QUESTIONS BY MR. SNIDOW:
Q. You don't -- well --
MR. MURDICA: Well, she was talking and you interrupted her again.
MR. SNIDOW: I didn't mean to.
QUESTIONS BY MR. SNIDOW:
Q. You said you don't have an opinion on that.
Go ahead.
A. I don't think in terms of the greatest achievement. I think in terms of careful science and diligent search for the truth, which I think was done in this instance and has been done in other instances.
Q. Okay. You can put that aside

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now.
Do you agree that for a variable to be a confounder, it needs to be a true cause of the outcome of interest?
A. I think I've -- I think that the true cause is what's giving me hesitation here.
Q. Yeah.
A. Because something can confound an association by a -- an overall association by, I would say, reducing the overall impact of the measure of association.
So I think it can have an impact without being the cause.
Q. And are you saying that there can be partial confounding?
A. Correct.
Q. That's what you're saying. Okay.
But even the partial confounding, the confounding agent needs to actually cause the outcome, right?
A. It needs to have an established, reliable, valid association with the outcome. Again, the cause concern -- the

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word "cause" concerns me because we will evaluate a confounder without knowing whether it's causal -- causally related. But if we see a reduction, we say it's a confounder.
Q. But isn't that just in an abundance of caution?
Like, in other words, you cast your net a little broader than the ones you think are actual cause just in case, right?
A. We cast a wide net if we have data on the potential confounders, we examine them, and we look to see what that does to the measure of association.
Q. Do you have Exhibit 605 in front of you?
A. If I can find it.
Q. And while you're doing that, let me give you an example I think will clear it up.
MR. MURDICA: Well, hang on. You can ask her to do one thing. You can't ask her a question while she's trying to --
MR. SNIDOW: She's just getting it.

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THE WITNESS: Okay. This is the --
MR. SNIDOW: 605?
THE WITNESS: -- Federal Judicial Center thing?
QUESTIONS BY MR. SNIDOW:
Q. Yeah. Just hold on for a second.
So I don't know what your favorite example of confounding is. Mine is gray hair color and mortality.
Is that a good one?
A. That's a pretty basic one, yeah.
MR. WATTS: I object.
QUESTIONS BY MR. SNIDOW:
Q. And the -- no hair.
And the confounder is, of course, age, right?
A. Correct.
Q. Right.
And so if you were doing a study on, let's say, smoking and mortality, you wouldn't need to control for gray hair, right?

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MR. MURDICA: Objection. Form.
THE WITNESS: Gray hair is a proxy for age, so --
QUESTIONS BY MR. SNIDOW:
Q. Right.
A. -- you would need to control for it in its true form.
Q. You need to control for age, right?
A. Right.
Q. If you control for age, you wouldn't also need to control for gray hair?
A. But should you control for gray hair, you would see a difference in the effect estimate, and then you would need to identify what that meant.
And that was my earlier point, that something can be suspected to be a confounder and can later be revealed that it's not that, it's associated with something else that the -- that is the actual confounder.
Q. Yeah. I was actually going to ask you that, too.
If you can't control for

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something directly, you can control for a correlate.
A. If you know what the correlate is, and you have data on that correlate --
Q. Yeah.
A. -- that's reliable and valid, you can enter that into the model to see if it makes a difference.
Q. So in other words, let's say I couldn't control for age in my study.
A. Yep.
Q. They just lost the data. But I had data on hair gray, it's not going to be a perfect measure of age, but it's still better than nothing, right?
MR. MURDICA: Objection to form.
THE WITNESS: It's a proxy for age, so...
QUESTIONS BY MR. SNIDOW:
Q. And that's one way of controlling for confounders that you can't see, is by controlling for proxies?
MR. MURDICA: Objection to form.

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THE WITNESS: I would agree that there are times when we don't have the exact data that we would like to enter into the model to see if it makes a difference, and we may use a proxy for that.
I think we need to understand how it might be approximately associated with the confounder we're thinking about, but, yes, I will grant you that.
QUESTIONS BY MR. SNIDOW:
Q. And one way you can control for confounders is using multiple regression models?
A. Correct.
Q. Another way you can control for confounders is by doing stratifications?
A. Correct.
Q. And just to walk through with our example, if I did -- if I did gray hair -- if I did, let's say, smoking and mortality and, you know, there was some age confounder, I could control for age, and then whether the association went away or not

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would determine whether there was actual confounding effect, right?
MR. MURDICA: Objection to form.
THE WITNESS: So I believe you're saying you would stratify on age and see if the effect estimate was the same in those two strata?
QUESTIONS BY MR. SNIDOW:
Q. Yeah.
A. That is one approach, yes.
Q. Okay. And then for multivariate regression, let's say -- what did I say, gray hair, mortality. And obviously we think the confounder is age.
The other thing I could do is I could just make a very long multivariate model that included age and see whether the association between gray hair and mortality stayed the same, right?
MR. MURDICA: Objection to form.
THE WITNESS: I'm not really following you because you told me that gray hair -- you didn't have

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information on age.
QUESTIONS BY MR. SNIDOW:
Q. No. No. Forget that one.
A. You said you'd use gray hair as a proxy.
MR. MURDICA: You can't wave your hand and talk in the middle of her answer. You keep doing it. Please, please. I'm asking you very kindly to stop.
QUESTIONS BY MR. SNIDOW:
Q. Let's say I did a regression of gray hair and mortality.
All right?
A. Okay.
Q. I would get an association.
A. Okay.
Q. Definitely spurious, right?
A. Okay.
Q. The way to test that, one way, would be to do a multivariate analysis and include age in my model.
A. Okay. I'm following you in that.
Q. Is that right?

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A. But you would -- before you did that, you would first look at the correlation between gray hair and age and see that they were very strongly correlated, and you might not enter them both into your model because that's not the way we do it.
But fair enough.
Q. Yep.
And my question was if we had my model and including age made the association go away, that would be good evidence that the association between gray hair and mortality was confounded, right?
MR. MURDICA: Objection to form.
THE WITNESS: If you added age to the model and your association with gray hair went away, you -- if you knew the correlation between gray hair and age, you could say that is serving as a proxy for age and it's no longer significant in the face of age, which is actually the variable that's driving the association.

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QUESTIONS BY MR. SNIDOW:
Q. Yep.
And similarly, if you control for something and the association doesn't change, that's good evidence that it's not confounding, right?
MR. MURDICA: Object to form.
THE WITNESS: I think that's a little trickier because it depends on the reliability and validity of the data for that confounder.
QUESTIONS BY MR. SNIDOW:
Q. Yeah.
A. So it could be that it doesn't change because it's an imperfect measure of the confounder. It could be that it doesn't change because the confounder is actually tied to something else that you haven't measured.
So I think it's a little easier to agree with the first and a little harder to agree with the second.
Q. But assume I had measured perfectly, perfect measurement of everything, I know it's not --

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A. I mean, theoretically.
Q. Yeah. Theoretically, a perfect measure for everything, if you control for something and the association doesn't change, that's evidence that whatever you're putting in the model is not a confounder?
MR. MURDICA: Objection to form.
THE WITNESS: Yeah. And, you know, this is -- this is so theoretical, and it's so unlikely, that it's hard to -- you know, it's hard to disagree with you, but it's also hard to agree with you because it's not -- it's not reality based.
QUESTIONS BY MR. SNIDOW:
Q. Well, that is why you do multivariate regression, right?
MR. MURDICA: Objection to form.
THE WITNESS: Again, it's why you do multivariate regression -- regression with good data. And here, you're talking about something that's completely hypothetical and

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impossible.
QUESTIONS BY MR. SNIDOW:
Q. Okay. Let's put genetics aside for a moment.
What causal risk factors do you think have not been controlled for in any of the studies looking at the relationship between prenatal APAP exposure and ASD?
MR. MURDICA: Objection to form.
THE WITNESS: So I'd have to go through the studies and look at the specific list of confounders. You know, each cohort study included a different set. I would tell you that none of them included all of the most important confounders that I would consider.
So I can't, off the top of my head, say MoBa didn't control for this, DNBC did, you know. I think I would have to look at it.
But I would say that none of them controlled for everything that might be relevant in that association.

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QUESTIONS BY MR. SNIDOW:
Q. Can you tell me any particular one? What specifically did they fail to control for across all of the studies, or any, if you want?
MR. MURDICA: Same objection.
THE WITNESS: I can't answer across all because, as I said, there are differences among the studies. I'll give you an example.
The Ji study, which used the -- Ji studies, which used the Boston Birth Cohort as a basis for their analysis, did not control for genetic confounding. And that's a very significant confounder and a very significant limitation, among others, of the results that they present.
QUESTIONS BY MR. SNIDOW:
Q. All right. Besides genetics, anything else?
A. So there are studies that, although they attempted to control for confounding by indication, based that control on very imprecise and imperfect maternal

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report of indications, and often that indication is not tied to the actual exposure of acetaminophen.
So an imperfect control for something that is a very important, underlying, methodologic challenge.
Q. All right. Anything else?
A. Those are the two big ones in my mind. As I've said before, genetics and confounding by indication are the two that I would say are front of mind when I'm reviewing these studies.
Q. So aside from those two, sitting here right now, you can't think of any causal confounder that was not controlled for across the studies?
MR. MURDICA: Object to the form.
THE WITNESS: Again, I would want to review the studies, review the confounders they considered, and give it the proper consideration before I answered that, you know, categorically.
But as I said, the two most

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important confounders were not thoroughly controlled in many of the studies.

QUESTIONS BY MR. SNIDOW:

Q. And sitting here right now, you can't think of any others?

MR. MURDICA: Object to form.

THE WITNESS: I've tried to answer that question. I said I'm unwilling to, you know, use memory and try to recall which ones were included and not included. I would want to review the studies and review the specifics of the confounders they collected, and the -- and the integrity of that data.

QUESTIONS BY MR. SNIDOW:

Q. Okay. You know that many of the study authors have said that confounding by indication is unlikely, right?

MR. MURDICA: Objection to form.

THE WITNESS: I would like to have you point to a specific citation. I've certainly seen that, but I

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don't -- are we done with this one, by the way? Because I pulled it out and we don't need it.

I don't necessarily agree with that characterization.

QUESTIONS BY MR. SNIDOW:

Q. Well, I'm pulling out a study now, but while they're doing that, I'm not asking whether you agree.

You know that a lot of the study authors have said, we've looked at the data; we don't think confounding by indication is very likely?

MR. MURDICA: Objection to form.

THE WITNESS: Again, I know that study authors have said that. And as I've just explained, the data on confounding by indication in many cases is imperfect at best. And so in my mind, it's overstepping the data to make a conclusion like that.

(Pinto-Martin Exhibit 615 marked for identification.)

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QUESTIONS BY MR. SNIDOW:

Q. Okay. So here's Ricci 2023, which I'll mark as 615.

A. Another meta-analysis?

Q. Yeah. Yes.

All right. And it sounds like you're familiar with this because you knew it was a meta-analysis, right?

A. I did.

Q. All right. And they say that "The objective of the study was to assess the extent to which the association is due to confounding by indication."

Right?

A. Correct.

Q. And that is one of the two things that you think is confounding this relationship; the other being genetics, right?

A. Uh-huh.

MR. MURDICA: Objection to form.

THE WITNESS: I agree.

QUESTIONS BY MR. SNIDOW:

Q. You agree.

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All right. So that's the objective of their study.

And then if we go to the conclusion of their study, they say, "Confounding by indication did not explain the association between in utero acetaminophen exposure and child ADHD."

Right?

A. So that is the box that's been pulled out on the second page of the article. And as often is the case, it's an oversimplified view of their final results.

Q. Okay. Hold on. Let's look at the final results then.

Let's go -- let's go to 9, Principal Findings.

And this isn't in the abstract anymore, right?

A. Correct.

Q. Okay. So it says here, "Principal findings are findings indicating a small to moderate association between in utero acetaminophen exposure and risk of child ADHD, which did not appear to be explained by confounding by indication."

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Did I read that correctly?
A. You did, and I think their language is important which did not appear to be explained by confounding by indication.
Q. Well, let's --
A. Can we turn to their conclusions?
Q. Let's first look at their chart.
So at the top, they actually do a forest plot, right?
A. They do.
Q. And they say that this forest plot is adjusted for maternal and infant characteristics and confounding by indication.
Right?
A. So they are relying on a set of studies that attempted to control for confounding by indication, and as I've said before, the data that they're relying on is imperfect.
We do not have a direct -- a direct piece of evidence on the indication for acetaminophen use and the timing of

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exposure relevant to that indication.
Q. Yeah.
A. And so they are using a set of data that's imperfect with respect to this potential confounder. They analyzed it anyway, and they were unable to demonstrate that it had an impact.
And in their conclusions, they state as much. So in their conclusions, I just want to point out --
Q. Yeah.
A. -- that they say, "However, the certainty of the evidence on this topic is low, and findings should be interpreted in light of the limitations of the existing studies," -- what I was just referring to -- "as well as the limited number of sufficiently comparable studies available to meta analyze. These findings strongly suggest the need for high-quality studies with adequate control for both measured and unmeasured maternal indications for acetaminophen use."
So they're saying we didn't have that, and that's what we need.

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MR. MURDICA: You talked three times during her answer there. You've got to try to stop. You did.
QUESTIONS BY MR. SNIDOW:
Q. Would you mind going to page 9?
MR. MURDICA: You're on video doing it. I'm trying to help you here.
QUESTIONS BY MR. SNIDOW:
Q. Do you mind going to page 9 that we were just looking at?
A. Yeah, I see it.
Q. My question was just going to be -- what I asked was, in their -- I know you think it was imperfectly done, but what they're saying is they produced this meta-analysis adjusting for confounding by indication, right?
That's what they say. I know you disagree, but that's what they say?
MR. MURDICA: Object to form.
THE WITNESS: Again, you're taking one line here, and they say that, and then they qualify it in their conclusions, which I would argue

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is one of the most important sections of any epidemiologic study.
Why? Because an honest epidemiologist will acknowledge, I did my best, and there are these problems that must be considered in order to evaluate the credibility of this evidence with respect to a causal -- hypothesized causal association.
QUESTIONS BY MR. SNIDOW:
Q. All right. Let me ask it a different way.
Did the Ricci meta-analysis conclude that there was confounding by indication that could explain this association?
A. Again, their pooled estimate does not support confounding by indication.
Q. Okay.
A. And yet they state that that data is imperfect and needs to be followed up with more precise and accurate data.
Q. That's all I wanted.
All right. Do you have the Alemany study in front of you?

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A. Remind me what number it was, if you remember. I can find it, I'm sure. Did you give it to me?
MS. BARRIERE: Try 612.
THE WITNESS: So mine goes from 611 to 613, so something happened to Alemany along the way. Let's see if it got misfiled.
Oh, here we go. I got it. It was just out of order.
QUESTIONS BY MR. SNIDOW:
Q. All right. Can you turn to page 1001?
A. (Witness complies.)
Q. Are you there?
A. 1001.
Q. You see where it says "however"?
A. Uh-huh.
Q. It says, "However, the consistent associations found across different sensitivity analysis, including examining ASC and ADHD diagnosis in the largest cohort, makes unlikely that the observed relationship between prenatal

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acetaminophen and ASC and ADHD symptoms is entirely explained by unmeasured confounding."
Did I read that correctly?
A. That is their statement.
Q. And do you disagree with these study authors too?
A. I do.
Q. You do?
A. I do.
Q. Okay. Have you -- have you written to them to tell them that they're very wrong on that?
MR. MURDICA: Objection to form.
THE WITNESS: I have not written any letters directly to authors, which I actually have never done, and I've not written a letter to the editor, which I have done in the past, because as I said, the past period of time, that has not been my focus.
QUESTIONS BY MR. SNIDOW:
Q. But you do -- you do disagree

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with these authors?
A. I do.
Q. Can I have H, which we've done?
Do you have Olsen and Liew in front of you? 609?
Do you have it?
A. I have it.
Q. All right. Turn to page 1395.
A. What is it -- oh, it's the first page. Okay.
Q. Uh-huh.
Do you see where it says "Several analytical methods"?
A. Uh-huh.
Q. It says, "Several analytical methods that aim to minimize confounding bias have been utilized in these studies."
Right?
A. That's what it says.
Q. And then it describes a propensity score match method?
A. Uh-huh.
Q. Sibling-controlled analysis?
A. Uh-huh.
Q. And negative control

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comparison?
A. Uh-huh.
Q. And it says they've all given consistent results, right?
A. That's what it says. I disagree with that statement.
Q. All right. Hold on.
And it says, "Providing additional evidence against confounding as the primary reason to explain away the possible fetal programming of acetaminophen on brain function in childhood."
Did I read that correctly?
A. You read it correctly, but I --
Q. Do you disagree with these study authors, too?
A. I do.
Q. Have you written to them?
MR. MURDICA: Objection to form.
You asked these same questions before the break.
THE WITNESS: As I said, I -- I've never written to a study author, and I have not written to the editor

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to describe my feelings about the study.

Again, I'm not ruling out that it's something that I might not do in the future. I have not done it to date.

MR. SNIDOW: And you're right, Jim. I forgot I did.

(Pinto-Martin Exhibit 618 marked for identification.)

QUESTIONS BY MR. SNIDOW:

Q. All right. I'm going to show you Bauer and Kriebel, which I will mark --

MR. SNIDOW: What are we up to, Christy {sic}?

COURT REPORTER: I don't know because I think one of them got marked out of order.

MR. SNIDOW: Okay.

COURT REPORTER: So I don't want to tell you one --

THE WITNESS: I have 617 as my last one.

MR. CHARCHALIS: You marked Surgeon General report as 617, and

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then you went back and you marked -- you marked the Nature in 1958 as 14 --

MR. SNIDOW: Uh-huh. Can I do --

MR. CHARCHALIS: -- and then you marked Ricci as 15, and you didn't do 16.

QUESTIONS BY MR. SNIDOW:

Q. Okay. This one is going to be 18.

A. Okay. So we're missing 16?

Q. Yeah.

A. That's why I was confused.

Q. All right. Do you see the Bauer and Kriebel article?

A. I do.

Q. If we go to page 134, do you see where it says "Together these nine studies"?

A. Ah, sorry, I'm not there yet. Okay. "Together these nine studies."

Q. Okay. "Together these nine studies and five cohorts provide a strong body of evidence suggesting neurodevelopmental effects of prenatal APAP

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exposure."

Did I read that correctly?

A. You did.

Q. And then two sentences later it says, "Several lines of reasoning suggest that bias, confounding and chance are not solely responsible for the observed relationships."

Did I read that correctly?

A. You did.

Q. And I know you -- you probably disagree with the study authors on that point, right?

MR. MURDICA: Objection to form.

THE WITNESS: So I agree -- I disagree with the study authors' review of the evidence with respect to its support of a causal association between acetaminophen and ASD or ADHD.

QUESTIONS BY MR. SNIDOW:

Q. Do you think this sentence is unreasonable, "several lines of reasoning suggest that bias, confounding and chance are not solely responsible"?

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A. Again, I'm not going to comment on the reasonableness or unreasonableness of a statement that is made in the middle of a review article. You know my opinion on the evidence and its support of a causal association.

And so I, therefore, agree with -- I disagree, sorry, with the authors --

Q. Okay.

A. -- and the conclusions.

Q. All right. Then they say there's evidence of a dose-response gradient, right?

A. I see that.

Q. And do you agree that there's evidence of dose-response in this literature?

A. I do not agree there's evidence of a dose-response. As I've mentioned before, I think the fragility of the dosing information where we have no information on actual dose, on actual timing of dose and duration of dose, renders it really virtually impossible to conduct a valid dose-response relationship.

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Nevertheless, many authors have tried to do it.
Q. Yeah.
You see where it says, "No associations were found with ibuprofen or other analgesic medications suggested specificity of the association with APAP"?
A. I do see that.
Q. And you know that there were studies that looked for a link between ibuprofen and neurodevelopmental outcomes?
A. I do know that, and importantly, we have to recognize that women are advised against taking ibuprofen during pregnancy, so they will substitute ibuprofen with, for example, another analgesic like acetaminophen.
And, therefore, the numbers who report ibuprofen use are very small, so we might have the problem of inadequate power to test the association.
In addition, the -- the dose of ibuprofen is even weaker than the dose and duration information that we have on acetaminophen. It's often characterized as a

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dichotomous yes or no.
Q. All right. Any studies that do show a link between ibuprofen use and autism?
A. Again --
MR. MURDICA: Objection to form.
THE WITNESS: -- as I said, the data is very thin and weak because women are just -- are advised not to take it, and so we have very few studies that even asked about it, and where they did, it was a yes/no.
So in my mind, that's not adequate to rule that out as a potential.
MR. MURDICA: When you're --
QUESTIONS BY MR. SNIDOW:
Q. I'm just asking, is there a study that showed a link between ibuprofen and autism? Can you name me that study?
MR. MURDICA: Objection to form.
THE WITNESS: There is not a study. That was not my point.

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QUESTIONS BY MR. SNIDOW:
Q. Sorry. That's all I wanted.
And same answer for ADHD?
MR. MURDICA: Objection to form.
THE WITNESS: The same issue arises with respect to ADHD, which is that women are advised not to take ibuprofen during pregnancy. Very few of them do, and we still have the problem with recall bias, and we have the problem with a yes/no measurement of exposure.
MR. MURDICA: We've been going an hour. When you're done --
MR. SNIDOW: Yep.
MR. MURDICA: -- with the line of questioning, if you want to take a break, we'd be good with that.
QUESTIONS BY MR. SNIDOW:
Q. So can you name me a study that showed a link between prenatal APAP use and ADHD?
MR. MURDICA: Objection to form.

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THE WITNESS: As I just said, that data is weak, and we do not have a study showing that.
MR. SNIDOW: Okay. Yeah. We can go off the record.
VIDEOGRAPHER: The time is 1:54 p.m., and we are off the record.
(Off the record at 1:54 p.m.)
VIDEOGRAPHER: The time is 2:07 p.m., and we are on the record.
QUESTIONS BY MR. SNIDOW:
Q. Okay. Dr. Pinto-Martin, have you found the studies showing a pre or post-pregnancy use of APAP is associated with the autism diagnosis?
MR. MURDICA: Objection to form.
You know she hasn't because she hasn't had a chance. If you want her to look on record, just tell her to look now.
QUESTIONS BY MR. SNIDOW:
Q. Have you -- were you able to look?
A. I believe that the question was

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just answered. I have not had time to look.
Q. Okay. You know, we're going to do this right now. Will you please look for me?
And I'll -- you know, you can take the time you like, but realize what I'm asking is prenatal APAP use, pre-prenatal APAP use and autism diagnosis, post-pregnancy use and autism diagnosis. Take a look at your report.
A. So you're asking me about a negative control exposure analysis that had autism as the outcome?
Q. Correct.
A. Okay. I will look in my report.
Q. Yeah.
A. So in reviewing my report, there is not a study that looks specifically at pre or post-pregnancy use and --
Q. For autism?
A. Autism. The studies that do that analysis have both autism and ADHD as an outcome, but their analysis was restricted to pre or post-pregnancy use and ADHD.

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Q. Okay. So no evidence that pre or post-pregnancy use of acetaminophen is associated with autism?
MR. MURDICA: Objection to form.
THE WITNESS: As I said, there's no data on prepregnancy or post-pregnancy use of acetaminophen and the impact of autism, only on ADHD.
QUESTIONS BY MR. SNIDOW:
Q. All right. And then for ADHD, it sounds like you just saw the Ystrom study or Liew 2019?
MR. MURDICA: Objection to form.
THE WITNESS: Yeah. There's Liew 2019. There's Ystrom. There's Stergiakouli. There's Trønnes, and there's Chen. I think those are --
QUESTIONS BY MR. SNIDOW:
Q. But the only two that have ADHD clinical diagnosis as the endpoint are Liew 2019 and --
A. And Ystrom.

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Q. -- and Ystrom; is that right?
A. Uh-huh.
Q. And both of those did not find an association between prepregnancy use or post-pregnancy use and ADHD?
A. Let me remind myself specifically what they found.
Q. Yeah.
A. Because there's also supplemental materials that need to be considered.
Where am I in my report? Okay. So...
Actually, I'd rather just look at the actual papers rather than try and find it in my report because I don't remember where it is.
Q. Well, I actually don't want you to read the entire Ystrom and Liew paper right now.
If you don't know off the top of my head, we'll do it a little bit later, okay?
A. Okay.
Q. All right. But am I correct,

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sitting here right now, you can't think of a study that showed that pre or post-pregnancy use was associated with ADHD as a clinical outcome?
MR. MURDICA: Object to the form.
She was looking at the study because there was something else she wanted to say about it. So if you stop her -- you can't have it both ways.
THE WITNESS: Yeah. I didn't say that. I said I'd like to look at the studies to refresh my memory about the specific findings.
So I'm happy to do that, but I'm not going to try and guess.
QUESTIONS BY MR. SNIDOW:
Q. All right. Can you go back to Bauer and Kriebel that we were just looking at before the break?
A. Okay. I have it.
Q. Can you turn to page 137?
A. Okay.
Q. It says, "There were consistent

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findings in the nine prospective cohort studies within five cohorts suggesting adverse neurodevelopmental outcomes in children following APAP use in pregnancy."

Do you agree or disagree?

A. I disagree.

Q. Okay. Then later in the paragraph it says, "The relatively modest risks may be the result of residual confounding, but the identification of dose-response gradients, trimester effects, specificity to APAP, biological plausibility, as well as the findings that show associations are not confounded by indication for use, argue against a spurious association."

Did I read that correctly?

A. You read that correctly, and I'd be happy to talk about each one of those and my disagreement with each one of those.

We've talked about already the problems with the dose-response gradient being based on very imperfect and flimsy information.

The same applies for the

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trimester-specific effects. Although it is couched as prospective in many cases, we're still asking women to recall their exposure for the prior, at least, trimester, if not further.

With respect to specificity to APAP, I think we talked about the lack of data on ibuprofen because women are advised not to take ibuprofen during pregnancy.

With respect to biological plausibility, I have not said, but I will say now, that I use biological plausibility to support the evidence in epidemiologic studies when I'm conducting a Bradford Hill analysis. And in the absence of strong and solid epidemiologic evidence, I am not willing or need to consider biological plausibility.

Q. Okay.

A. And --

Q. My question was just going to be, do you agree or disagree?

MR. MURDICA: Did you finish your answer?

THE WITNESS: I think I finished.

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QUESTIONS BY MR. SNIDOW:

Q. Okay.

A. And I disagree.

Q. You disagree.

A. Which I said.

Q. With these authors here. All right.

A. Are we done with this one? I'm just trying to keep things in order.

Q. Yep. You can put it right there. Yep. Yep.

(Pinto-Martin Exhibit 619 marked for identification.)

QUESTIONS BY MR. SNIDOW:

Q. Showing you the label for valproic acid, which I will mark as 619.

There you go. Jim.

And have you read this?

A. I have not read the label for valproic acid. I'm not an expert in labeling, and it's not part of what I was asked to do in my review of the epidemiologic literature. So the answer is no.

Q. So before giving an opinion on valproic acid in your report, you didn't read

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the label?

MR. MURDICA: Objection to form.

THE WITNESS: There would be no reason for me to read the label when I'm reviewing epidemiologic studies. It's not what I do.

QUESTIONS BY MR. SNIDOW:

Q. Okay.

A. I'm not an expert in labeling.

Q. I just thought you might have been curious.

MR. MURDICA: Objection to the form and the commentary.

QUESTIONS BY MR. SNIDOW:

Q. Could you -- could you go to page -- so this one is hard to get to because the FDA did not put page numbers on here.

A. Of course not.

Q. But it's before -- if you find -- flip through and find Section 8.2, which is called Lactation.

A. 6.4.

MR. MURDICA: Here, if you want to use this one.

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MR. SNIDOW: Yeah, you can use Jim's.
THE WITNESS: If I can find the beginning. You did such a quick job of that.
QUESTIONS BY MR. SNIDOW:
Q. And then flip just to the previous page.
A. Okay.
Q. Do you see the paragraph that begins "Although"?
A. I do.
Q. It says, "Although the available studies have methodological limitations, the weight of the evidence supports a causal association between valproate exposure in utero and subsequent adverse effects on neurodevelopment."
Did I read that correctly?
A. That's what it says.
Q. Do you agree?
A. Again, this is a label. I have absolutely no idea how a label is created. I have no idea what data they are relying on when they make this statement, and so I --

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it's not part of my review of published epidemiologic literature, peer-reviewed literature, so I don't -- I'm not going to opine on whether I agree or disagree with something that is not something I've -- I typically review as part of my practice.
Q. Well, do you see where it says "ADHD" here?
A. I see that it says "ADHD."
Q. And "Autism Spectrum Disorders"?
A. I do.
Q. Do you agree -- I'm not asking about the label, just do you agree with the sentence, "The weight of the evidence supports a causal association between valproate exposure in utero and subsequent adverse effects on neurodevelopment, including ASD and ADHD"?
MR. MURDICA: Objection to form.
THE WITNESS: Again, we've talked about my opinion with respect to valproic acid with respect to ASD and ADHD, and that there's interesting

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evidence that supports the causal hypothesis, but I still think there is work to be done because of methodologic limitations of the study.
And, in fact, these authors, whoever they may be, acknowledged those methodologic limitations right at the outset of their statement.
QUESTIONS BY MR. SNIDOW:
Q. Well, the authors are the makers of valproic acid, right?
A. I have no idea. Again, I don't know how labels are created.
Q. You don't know that they're approved by the FDA?
MR. MURDICA: Objection to form.
THE WITNESS: I don't know how labels are created. It's not an area that I've learned anything about. It's not an area I care to learn anything about. It's not part of what I do as an epidemiologist. It's not part of my review of the peer-reviewed, published literature.

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QUESTIONS BY MR. SNIDOW:
Q. Okay. I think, when we were talking before, you told me you've -- you weren't sure but you thought cause was most likely for valproic acid.
Are you changing your testimony?
MR. MURDICA: Objection to the form.
THE WITNESS: I believe what I said before, is that there is interesting suggestive evidence of a potential causal link and that the methodologic flaws in the study, in my mind, mean that we still have work to do, both for -- with respect to ASD and ADHD.
QUESTIONS BY MR. SNIDOW:
Q. Oh, I know there's more work to do, but do you think the weight of the evidence supports a causal association or not?
MR. MURDICA: Objection to the form.
THE WITNESS: Again, I'm --

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that was not part of my assignment, was to -- you know, I was not asked to review the evidence on valproic acid. I was asked to review the evidence on acetaminophen and ASD and ADHD. I'd be happy to talk to you about my assessment of the body of evidence with respect to that.

Valproic acid was in my introduction to the epidemiology of autism and my introduction to the epidemiology of ADHD as a medication that has been studied, and I think I was clear on my feeling about the body of evidence that I reviewed with respect to that.

QUESTIONS BY MR. SNIDOW:

Q. You don't remember telling me it was most likely causal?

MR. MURDICA: Objection to the form.

THE WITNESS: I remember a series of questions that you asked about trying to rule out confounding and bias, and I don't remember

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precisely what I said, but I will state again that I think that there is interesting evidence and it needs to -- and it's certainly stronger than the evidence for acetaminophen and prenatal exposure to acetaminophen and ASD or ADHD because of the important issue of certainty of timing and dose and exposure because we have medical records confirming that.

And also certainty about the indication for use because we have medical records confirming that as well.

QUESTIONS BY MR. SNIDOW:

Q. For ADHD, the evidence consisted of five small studies and a meta-analysis; is that right?

MR. MURDICA: Objection to form.

THE WITNESS: For valproate?

QUESTIONS BY MR. SNIDOW:

Q. Uh-huh.

A. I would want to go back and remind myself exactly what the body of

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evidence was. Again, that was not the primary focus of my review.

Q. You just got -- you've got two sections on valproic acid in your report, don't you?

MR. MURDICA: Objection to the form.

THE WITNESS: I have two sections. One in the background on ASD, and one in the background on ADHD.

QUESTIONS BY MR. SNIDOW:

Q. What's valproic acid indicated for?

A. My understanding -- again, I am not a clinical doctor, but my understanding is that valproic acid is used to control seizures in a woman who has seizure disorder. It's used as a prophylactic, I believe, for someone who has migraine headaches, and there may be a couple other indications for use.

Interestingly, seizure disorders are also implicated in autism spectrum disorder. And so there may be -- one of the reasons that we need to continue

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to study it is that there may be a genetic confounder in there that both increases the risk of seizures and increases the risk of autism in the offspring, and I think we need to continue to look at that.

Q. Well, Depakote indicated for acute treatment of manic or mixed episodes?

A. Again, I'm not an expert on valproate. I don't know how it's used. You read that sentence correctly. I have -- I don't know. What are you asking?

Q. I'm asking, do you think to know whether confounding by indication has been controlled for you need to know what the indication is?

A. I think that I understand the primary indications for use of valproate, and the studies that I've looked at looked at it in relation to seizure disorder and migraine.

Q. Okay. But do you see here the FDA is saying it's indicated for acute treatment of manic or mixed episodes?

A. I see that that's on this paper. Again, it's not something I reviewed, and it's not something that the literature

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that I reviewed discusses.
So it's not relevant to my opinion because I didn't see any evidence for or against that as an indication.
Q. Well, that's kind of my point, though.
Don't you think that a drug that's -- that's indicated for manic episodes and bipolar disorder or psychotic features, that raises some pretty serious confounding by indications concerns, right?
MR. MURDICA: Objection to form.
THE WITNESS: Again, I do not have knowledge of the specific indications -- for all of the specific indications for use for valproic acid. The literature I reviewed did not address manic or mixed episodes in their analysis, so I don't -- I can't comment on it. I'm an epidemiologist. I rely -- I rely on published epidemiologic literature.
QUESTIONS BY MR. SNIDOW:
Q. All right. Can you look at your report, please?
A. Uh-huh.
Q. And can you go to page 35?
A. I'm there.
Q. Okay. You see "valproic acid"?
A. I do.
Q. Do you see that you report the indication there?
A. Epilepsy, manic episodes, prophylactic -- yes.
Q. So you did note that manic episodes is an indication for valproic acid, right?
MR. MURDICA: Objection to the form.
THE WITNESS: I -- yeah. I -- I'm -- forgot that that was one of the indications, but it does say that, yes.
QUESTIONS BY MR. SNIDOW:
Q. Do you agree that raises grave confounding by indication concerns?
MR. MURDICA: Objection to the form.
THE WITNESS: I would agree that all of them do, in fact.
QUESTIONS BY MR. SNIDOW:
Q. Yes.
A. Epilepsy and seizure disorder, which I guess is equivalent to epilepsy, and migraine headaches, because they all have an independent association with an increased risk of autism spectrum disorder, which is precisely why I'm not willing to say, ah-ha, we found something that is definitely causally associated. I think there may be confounding that we still need to address, which is -- and I -- and I think I've said that; that there's methodologic challenges that need to be continued to -- we need to continue to study.
Q. And did you say that in your report, what you just told me?
MR. MURDICA: Objection to form.
THE WITNESS: With respect to valproic acid?
QUESTIONS BY MR. SNIDOW:
Q. Yeah.
Can you just take a look at that paragraph? Because you're giving me a lot of, I don't know how strong this is, confounding.
Is that in your report?
MR. MURDICA: Objection to the form of the question.
THE WITNESS: Again, that was not the purpose of my report.
The purpose of my report to -- was to evaluate the epidemiologic evidence with respect to APAP exposure and ASD and ADHD. This section of my report is background information on the etiology of autism spectrum disorder. I did a similar section, background on the etiology of ADHD, and I'm reflecting on published literature that has interesting and worthy of consideration findings, valproic acid being one of them.
QUESTIONS BY MR. SNIDOW:
Q. Well, you say it's stronger than the association here, right? You say that in the paragraph?
A. It's stronger than the

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association we have with APAP.
Q. And do you ever, in this paragraph, mention that you have concerns about genetic confounding or confounding by indication for valproic acid?
MR. MURDICA: Objection to the form.
THE WITNESS: I tried to answer that question already by describing that this was not the primary focus of my report. This was background information about ASD in this case, ADHD in the other case. And the primary literature that I reviewed was the focus of my discussion of confounding by indication and confounding by genetics.
QUESTIONS BY MR. SNIDOW:
Q. Are you aware of any paper that was able to conclusively rule out confounding by indication for valproic acid?
MR. MURDICA: Objection to form.
THE WITNESS: I am not aware of a paper that was able to do that.

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QUESTIONS BY MR. SNIDOW:
Q. Were you able -- sorry.
Can you tell me a paper that was able to conclusively rule out confounding by genetics for valproic acid?
A. I cannot tell you a paper that was able to conclusively rule that out because we don't understand the total picture of genetics, and that is precisely why I'm saying we need to do additional studies.
Q. Need to do additional studies before making a causal inference?
A. Need to do additional studies to understand the causal pathway that exists, if it does, linking valproic acid to ASD or ADHD. We need to understand the way that the causal pathway operates.
Q. Well, I know. Here's what I'm asking.
Given that you couldn't rule -- there's no study ruling out confounding by genetics or confounding by indication. Do you think that the makers of valproic acid were right to say, the weight of the evidence supports a causal association?

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Do you think that was right or wrong?
A. Again, I'm not willing to comment on a label. A label is not something that I review typically. I don't know what's expected in a label. I don't know what literature they reviewed here. You're pulling out one sentence from a long document, and I'm just not willing to comment on it.
It's not my area of expertise. It's not what I was asked to do in this engagement.
Q. What if I put the sentence in a document that's not the label? Can you tell me if you agree or disagree with the sentence?
A. Again, I think context matters, and I'm not going to give you a "yes" or "no" on something that is completely acontextual.
(Pinto-Martin Exhibit 620 marked for identification.)
MR. SNIDOW: Okay. Can I have AA?
THE WITNESS: I didn't get this

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one marked. Does that matter? We didn't mark this one.
MR. SNIDOW: I did. Someone else has got the marked one.
MR. MURDICA: Oh, remember, I turned you to the right page.
THE WITNESS: Oh, right. Sorry.
QUESTIONS BY MR. SNIDOW:
Q. All right. I'm going to show you Wiggs, which is valproic acid paper that you cite in your report. 620.
Do you see this paper?
A. I see this paper.
Q. And is that footnote 66 in your report?
A. It is, Wiggs, yes.
Q. And this was published in, it looks like, 2020?
A. That's correct.
Q. So pretty recently?
A. That's pretty recently, yes.
Q. And if you go to E 233.
A. Uh-huh.
Q. You say, "The majority of

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research does not adjust for many, if any, confounding factors."

Correct?

A. That's correct.

Q. It looks like severity of maternal epilepsy. It seems like a good one to adjust for, right?

MR. MURDICA: Objection to form.

THE WITNESS: I think epilepsy is an important potential confounder. I think severity would be also a relevant --

BY MR. SNIDOW:

Q. Yeah.

A. -- addition.

Q. If you go to E 3238, you see where it says, "We were not able to adjust for parental diagnosis of ASD and ADHD"?

A. Sorry. I just -- third, we were not able -- yes, I see that.

Q. That's a pretty important thing to adjust for, right?

A. I believe that parental diagnosis, which would reflect a heritability

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estimate, is important, yes.

Q. But they didn't have it here for valproic acid, right?

A. They did not, I guess.

Q. And it says, "Given these disorders are heritable, this is a likely source of confounding in the present study."

Right?

A. That's what they say.

Q. So more than just saying they weren't able to rule it out; they're saying that confounding by genetics is actually likely for valproic acid, right?

A. Well, that's not -- I mean, they're not saying that. They're saying that they think that they should control for it, but they don't say likely. They don't use that term, so they think it's important.

Q. Okay. Any sibling studies for valproic acid that you're aware of?

A. I have not seen a sibling study on valproic acid.

Can I just point out that sibling studies are actually very challenging to do? You need a very large cohort --

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Q. Yep.

A. -- and able -- in order to be able to pull out the relevant sibling pairs, which have to be discordant for both exposure and outcome.

So I don't know how common valproic acid is prescribed, but my guess is it would take an enormous cohort with a long follow-up period of multiple family members to be able to actually do a sibling-controlled analysis.

Q. And why do you need such a big cohort for sibling-controlled studies?

A. I just described that the relevant data for a sibling-controlled study is those individuals who are divergent on both exposure and outcome.

So you can imagine how the numbers drop down once you are restricting to that. It's -- that's basically a matched analysis, and only two cells of that 2 by 2 table are relevant to the question at hand.

Q. And what happens when that number of discordant pairs gets too low?

A. Well, I will say that in the

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one sibling-control study that we have for ADHD, Gustavson, the numbers went from, you know, over 100,000 women down to something like 3 -- 300-plus who were discordant on exposure. However, they were able to demonstrate an attenuation of the risk to the null.

The problem we worry about with small numbers is the probability of a type 2 error of missing an association, right? But if we were able to demonstrate an attenuation to the null, it wasn't a problem in that study.

Q. Well, let's say that I tried to do a sibling-controlled study with five discordant pairs.

Okay? Do you understand the hypothetical?

A. Five discordant pairs --

MR. MURDICA: Objection to the form.

BY MR. SNIDOW:

Q. Yeah.

A. -- on outcome?

Q. Yeah.

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A. On exposure and outcome?
Q. Exposure on outcome -- and outcome, the relevant data.
A. Okay.
Q. Almost certainly going to get a null result, right?
A. I have no idea. It totally depends on what exposure you're talking about, what outcome you're talking about.
Q. On five? If it's five siblings, you think I'm going to get a statistically significant result?
A. Again, I'm not going to try and guess what the statistical result would be based on an entirely hypothetical result. We have a real result here --
Q. Yep.
A. -- with 34 discordant pairs, which is at least equal to 68, probably more, because there's more than one sibling in some cases, and we were able to see an attenuation to the null.
So that study had the statistical power to demonstrate confounding by genetics.

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Q. Well, you said the only concern is type 2 indication, but if the study gets small enough, there's going to be a type 1 problem, too, right?
A. Theoretically, I -- again, we don't have data on that, and there's no point in talking about it without having data on that.
Q. But theoretically, what I said is true?
A. I mean, we don't -- that's not the situation. We have -- we have --
Q. We'll talk about Gustavson. I just want to know, theoretically you get too small of a sibling control, you're going to get a type 1 error, right?
MR. MURDICA: Objection to form.
THE WITNESS: I guess I would ask a statistician that question.
I've never done a sibling-control with five.
QUESTIONS BY MR. SNIDOW:
Q. Yeah.
A. Nor would I.

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Q. You wouldn't.
All right. For ADHD and valproic acid, are you aware of any studies that showed a risk ratio of more than 2.0?
A. Not in my recollection. Again, this was not the main focus of my report, so I don't have a strong recollection of a study that I reviewed, but I don't remember a risk ratio that high.
Q. Are you aware of any studies for valproic acid that were able to rule out confounding by indication?
A. I would want to look at the studies that I cited to to see if any of them attempted to do that. I don't recall specifically.
Q. All right. Give me CC.
If you look at your report, you cite one study. It's Christensen 2019.
A. We're talking about --
Q. ADHD.
A. -- valproic acid and ADHD now?
Q. Yeah.
A. Okay. So we're off of Wiggs?
Q. That's right.

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It's on page -- it looks like 73.
Do you see a footnote 185?
A. I do.
Q. All right. And that's Christensen?
A. And then I cite again to Wiggs.
Q. Yeah.
You say, "Regarding valproic acid exposure, a 50 percent increased risk of ADHD was reported"?
A. Yes.
Q. That's a risk ratio of 1.5?
A. Correct.
Q. And then it looks like there's a meta-analysis --
A. Uh-huh.
Q. -- that had a null finding?
A. That was -- yeah. That was a meta-analysis, similar to these meta-analyses in the APAP literature, that had a range of neurodevelopmental outcomes, not just ADHD.
Q. Well, it's not similar because they had a null finding, right?

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MR. MURDICA: Objection to the form.
THE WITNESS: Well, some of these studies had a null finding as well.
QUESTIONS BY MR. SNIDOW:
Q. You've got a meta-analysis for me that had a null finding in this literature?
MR. MURDICA: Objection to the form.
THE WITNESS: We've discussed some of the meta-analyses, and although they report a small statistically significant elevated risk, they are quick to point out that they -- the result could be confounded due to the heterogeneity of the outcome, due to the misclassification of exposure.
So a null finding is one outcome that we need to be concerned about, but a positive finding with a qualification of the authors themselves about the reliability of

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that finding is something that I take into consideration.
QUESTIONS BY MR. SNIDOW:
Q. I know, but you said, well, some of these meta-analyses here had a null finding as well. That's what you said, right?
A. I'm talking about the --
Q. Sorry. Can you focus on my question?
MR. MURDICA: Whoa, whoa.
MR. SNIDOW: Yeah, she's not answering this one.
MR. MURDICA: You're interrupting her again.
MR. SNIDOW: I know, but she's not being responsive, and you know it.
THE WITNESS: I'm sorry. I'm not understanding your question.
QUESTIONS BY MR. SNIDOW:
Q. You said --
A. I'm not trying to be nonresponsive.
Q. -- well, some of the meta-analyses here had a null finding as

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well. That's not true. You don't have any meta-analysis in this literature that had a null finding.
MR. MURDICA: Objection to the form.
THE WITNESS: I tried to answer the question by pointing out that although the meta-analyses report an elevated association, they are based on studies that are heterogenous with regard to outcome, that are based on studies with imperfect measure of exposure.
So in my mind a meta-analysis is only as good as the underlying data, and as I pointed out repeatedly here, the underlying data is exceedingly weak.
QUESTIONS BY MR. SNIDOW:
Q. Okay.
A. I have to respond to one text. I apologize. It's important.
(Pinto-Martin Exhibit 621 marked for identification.)

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QUESTIONS BY MR. SNIDOW:
Q. Okay. I'm going to show you Christensen 2013, which is 621. 2019, sorry. I said it wrong. That's the one I want. Yep.
Could you turn to page 9?
A. I'm sorry, I have different paging I think than you do. Limitations --
MR. MURDICA: It's 9 of 13. There's a slash there. There.
THE WITNESS: Oh, I see. I thought it was 913. Got it. Okay.
QUESTIONS BY MR. SNIDOW:
Q. Do you see limitations at the top?
A. I do.
Q. Do you see where it says, "Due to the observational nature of this study, we cannot rule out that the observed risk increase for ADHD is at least in part explained by the mother's health condition that triggered the prescription of valproate during pregnancy"?
A. I do see that.
Q. Fair to say they're describing

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confounding by indication there?
A. Or perhaps comorbid conditions, yes.
Q. Yeah. Some kind of confounding?
A. Uh-huh.
Q. And they're saying they can't rule that out?
A. That's correct.
Q. All right. Do you see here it said for their dose data that they estimated the average daily dose?
A. I do see that.
Q. And that's how they did their dose-response?
A. And I've never quibbled with the dose-response with respect to valproic acid, if that's where you're going, because as I've stated, they have data because it's a medication that requires prescription.
They have data on dose and timing and duration, which we do not have in the acetaminophen literature.
Q. Oh, I actually didn't under -- I misunderstood your report.

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You think it's actually okay to use average daily dose to do a dose-response so long as you have really good data on average daily dose?
MR. MURDICA: Objection to form.
THE WITNESS: If you can actually quantify dose, then I think there is nothing wrong with creating a measure of that actual data on dose that equates with estimated average daily dose.
To do that on the basis of self-report that is retrospective, I have a problem with.
QUESTIONS BY MR. SNIDOW:
Q. Okay. The conclusion here, they note that "a randomized clinical trial is neither feasible or ethical."
A. I see that, and I agree.
Q. And you agree?
A. I do.
Q. Yep. It says, "Replication of our findings in large-scale observational studies is warranted."

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A. And I said that right from the start, that we need more data on this. We need more studies. We need continued examination.
Q. More data before what? Before warning women about the risk of valproic acid?
A. More data to understand what the causal pathway is, so I wouldn't even go to the next step. We need to understand the causal pathway.
That's what epidemiology does. That's why it evolves over time. That's why the studies become more sophisticated.
As we identify confounders and we're able to gather data to control for those confounders, we have a more effective assessment of the link between exposure and outcome.
(Pinto-Martin Exhibit 622 marked for identification.)
QUESTIONS BY MR. SNIDOW:
Q. All right. I'm going to mark a document as 622, which is a transcript. Thank you.

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All right. Do you know what the National Center for Toxic -- Toxicological Research is?
A. I don't. It's a national center that must study toxicology, but I have no knowledge of it.
Q. You don't even know what that is?
A. I -- as I said, I have no knowledge of it.
Q. All right. Do you know what a science advisory board is?
A. I do know what a science advisory board is.
Q. What's that?
A. It's a group of individuals that are either volunteered or paid to serve on -- as a review for a company, an organization, an institute, any number of those.
Q. If you turn the page, it's got a list of attendees, and one of them is division of neurotoxicology, John Talpos.
A. I see that.
Q. Do you know that guy by any

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chance?
A. I have not ever met John Talpos.
Q. If you turn to page 36.
And do you see here where it says, "So there's a growing concern about the potential toxicity of in utero exposure to acetaminophen"?
A. I see that.
Q. And then it goes on to talk about the 2021 consensus statement.
A. I see that.
Q. And you know what that is, of course, the Bauer --
A. I know that that's -- they -- it's called a consensus statement. I have some quibble with that title, but, yes, I know what it is.
Q. And then it says, "The concerns over APAP are being driven by a series of high-quality epidemiological studies."
A. I see that's what these authors stated.
Q. Would you agree?
A. So I think that the cohort

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studies that were designed, not for the purposes of looking at APAP exposure and neurodevelopmental outcome, were thoughtfully constructed and did a good job trying to collect data that they thought might be relevant to some potential hypothesis that they had not yet identified.
So they are strong epidemiologic studies for a very general purpose. They are not strong, high-quality epidemiologic studies for the purpose of evaluating exposure to APAP during pregnancy and ASD or ADHD.
Q. Do you see here he's saying the concerns over APAP?
A. I see that's what they say.
Q. And do you disagree?
A. I disagree that these are high-quality studies with respect to the question at hand of prenatal exposure to APAP and neurodevelopmental disabilities. They were not designed for that purpose, and so they are not high-quality for that purpose.
I'm not disagreeing that they're high quality for other purposes.

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They're not high quality for this purpose.
Q. Okay. So you disagree with John Talpos here?
A. I do.
Q. Okay. Then it goes down to say -- it talks about the cumulative sample size in the study.
A. Uh-huh, I see that.
Q. And it says, "It's an impressive dataset highlighting this potential concern."
Right?
A. It says they're really very big.
Q. That's what I was going to say. There's no dispute that they are monster datasets, right?
MR. MURDICA: Objection to form.
THE WITNESS: The size of these cohort studies is substantial, partly, I might point out, because they did not have a hypothesis to start. So they were casting a wide net and they were saying, let's collect a lot of

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information, and we will mine that information later with specific hypotheses, which is what they're doing now.
So the size of the study doesn't really matter if the data that they're trying to extract from those studies is imperfect to address the question at hand. And that's what I'm arguing.
QUESTIONS BY MR. SNIDOW:
Q. But in terms of cohort size, I think the Liew cohorts are about 60,000?
A. Again, I'm not disputing that they're large studies. It's -- the size of the cohort, frankly, doesn't matter if the data that they're using to derive the estimate of APAP exposure and neurodevelopmental outcome is weak or flawed.
Q. All right. Let's go to page 52 of this. Sorry, it's 51.
Do you see where he says, "Based on what we know, it crosses the placenta and blood-brain barrier quite readily"?

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A. I see that.
Q. Do you agree that APAP does cross the placenta and blood-brain barrier quite readily?
A. I've certainly read evidence to that effect. So I'm not a toxicologist so that's not my area of expertise, so I can't really comment. I don't know what "readily" means, but...
Q. Fair enough. You can put that one aside.
In your report you say that the association between ADHD and APAP exposure is highly inconsistent, right?
A. That's correct.
Q. In fact, you say it's hard to imagine any greater level of inconsistency?
A. I think those are my words. I'd like to --
Q. Page 59 of your report.
A. Yeah, that sounds like me.
Q. Yeah.
A. Yes.
Q. And do you stand by that?
A. I do.

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Q. And the reason that you say that -- they're inconsistent, if you turn to page 101 of your report, you do a comparison of some of the results in the literature.
Do you see that?
A. Yeah, this is a comparising -- comparing Liew 2014 and Ystrom 2017 with respect to their trimester of exposure data. Yeah.
Q. And the comparison you're doing with the red and the black is you're highlighting the ones that are statistically significant in black and the ones that are not in red?
A. That's correct.
Q. And that's why you say the results are inconsistent?
A. It's part of the reason I say the results are inconsistent.
Q. Yeah.
If you look above, it says, "A comparison of the adjusted results demonstrates that the results are inconsistent with statistically insignificant results in bold red."

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A. That is what I say.
Q. Let's look at -- you see it says, "Under any two trimesters for Ystrom," there's a 1.21 and a 1.20?
A. 1.21 -- I see 1.2 -- oh, yes. Okay. Got it.
Q. And you're suggesting that those two results are inconsistent with one another?
A. So when I'm evaluating consistency, I'm looking at a number of things. So, first of all, I'm looking at the pattern across trimesters, between two studies that relied on different datasets and, frankly, slightly different outcomes because one is looking at hyperkinetic disorder and one is looking at attention-deficit/hyperactivity disorder.
The pattern is somewhat variable. The statistical significance of the reported associations is somewhat variable and most importantly, the data that underlies those evaluations is inconsistent across the two cohorts and also potentially flawed.

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So inconsistency, in my mind, encompasses an understanding of the underlying data and the quality of that data. It's not just about a number. In this example I'm citing numbers, but my overall evaluation includes all of those things.
Q. I get it.
But in this example, you're citing the difference in significance between those two numbers, right?
A. I'm citing the difference across the two studies with respect to their findings by trimester.
Q. Well, no, I'm actually focused -- look at Ystrom. One study, Ystrom.
Do you see there's a 1.21?
A. Which is not statistically significant. I'm sorry, which is, and then a -- and then a 1.20, which is not. Sorry.
Q. Yeah.
A. Yeah.
Q. Yeah.
A. That's, again, one piece of the overall inconsistency. I'm talking about the

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pattern of associations that I see across trimesters.
Q. I know you're trying to say that you're not saying those are inconsistent now, but that's why you highlighted them in red and black, right?
MR. MURDICA: Objection to form.
THE WITNESS: So the point of this illustration --
QUESTIONS BY MR. SNIDOW:
Q. Go ahead. I'm just looking for my tabs. I'm sorry.
MR. MURDICA: She can't answer while you're talking to somebody else.
QUESTIONS BY MR. SNIDOW:
Q. Okay. Go ahead. The point of the illustration?
A. The point of the illustration is to look at the patterns of association by trimester derived from two different cohort studies.
That one -- the two lines that you pulled out are from within a single cohort, and I would argue one is significant

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and one is not, but that is not the basis for my statement that the results are inconsistent across the two cohorts.
Q. Let's look at page 5 of your report. Go back to page 5.
And do you see where you say, "Even ignoring issues of confounding and bias that most studies fail to address, the results across the studies of ASD and ADHD are inconsistent"?
A. I do.
Q. All right. So here you're ignoring issues of confounding and bias, right?
MR. MURDICA: Objection to form.
THE WITNESS: So for the purpose of describing statistically significant inconsistency, yes, but never in overall analysis would I ignore those issues.
QUESTIONS BY MR. SNIDOW:
Q. No, of course.
And then you say, "Some report statistically significant associations,

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others do not."
Right?
A. Correct.
Q. And that's why here, at least, you're saying that the results are inconsistent?
A. That's one factor that I consider when I'm looking at the criterion of consistency.
Q. All right. Can I have the book for a second?
Have you seen this? Rothman?
A. Rothman, yes.
Q. Fair to say this is one of, if not the, most authoritative texts in your field?
MR. MURDICA: Objection to form.
THE WITNESS: It's a good textbook on epidemiology.
QUESTIONS BY MR. SNIDOW:
Q. And described as the Bible by some?
MR. MURDICA: Objection to form.

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QUESTIONS BY MR. SNIDOW:
Q. Is that right?
A. I have no idea. I've never heard it described as the Bible.
(Pinto-Martin Exhibit 623 marked for identification.)
QUESTIONS BY MR. SNIDOW:
Q. Okay. I'm going to mark 623.
And this is a printout of, obviously, not the whole book for obvious reasons, but a couple of pages I want to talk about.
If you could please turn to --
A. Nice big paper on this one.
Q. Yeah, it's a PDF printout.
-- page 66.
A. Yes.
Q. And you see here Rothman says, "One mistake in evaluating consistency is so common and yet wrong that it deserves special mention."
Do you see that?
A. I do.
Q. "It is sometimes claimed that a literature or a set of results is

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inconsistent simply because some results are statistically significant and some are not."

Right?

A. Uh-huh.

Q. It says, "This sort of evaluation is completely fallacious."

Do you see that?

A. I do.

Q. Do you agree with that?

A. I think it's a bit strong, and I think that there are counterarguments to the value of using statistical significance as a way to evaluate the literature. I have a citation in my report to a recent JAMA article that describes the importance of holding to the standard when we're evaluating evidence, and I would say that in the case of imperfect data, it's even more important to consider the role of statistical significance. It will never be the only criterion by which I evaluate consistency, but I think given that we're looking at a multitude of different outcomes in this literature and different ways of assessing and combining exposure to determine dose, the

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likelihood of error is high.

And so I think that completely fallacious is a strong statement. And if we were talking about a very robust and carefully measured exposure and outcome, it would be a different story.

Q. And the reason you're saying you think completely fallacious is strong is because this is what you have done in your report. You've said the results are inconsistent because some are statistically significant and some are not?

MR. MURDICA: Objection to the form.

THE WITNESS: I made that statement, and I also made a -- I contextualize it to say that that is part of my criterion for evaluating consistency in a body of literature. I don't ever evaluate a single study in its -- on its own. That's not the way epidemiology proceeds, and so to look at the arc of evidence over time and the inconsistency of findings over time is very important.

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So, for example, the fact that one of the more robust designs to address the issue of confounding by genetics, the sibling-control design, which is one of the last studies we have published on this topic, was able to attenuate the result to the null, is very important in my consideration of the overall weight of evidence, if you will, with respect to APAP exposure and neurodevelopmental outcome.

QUESTIONS BY MR. SNIDOW:

Q. I promise I will talk about Gustavson with you.

My question was just, in part, your analysis of consistency is doing exactly what Rothman says is completely fallacious, right?

MR. MURDICA: Objection to form.

THE WITNESS: Again, this is a textbook. This is a teaching instrument that we use to describe to students how a -- an analysis with

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integrity should proceed. And the nuance of the underlying data is completely absent here.

So I would agree overall if all you're doing is looking at statistical significance out of context, then this statement is -- could be interpreted differently.

I'm saying that I do not believe that the way I conducted my analysis was completely fallacious because it was contextualized in the literature itself.

QUESTIONS BY MR. SNIDOW:

Q. Let me just ask it this way.

You did this in your report?

MR. MURDICA: Objection to form.

QUESTIONS BY MR. SNIDOW:

Q. You did that?

MR. MURDICA: Asked and answered.

THE WITNESS: I believe I tried to answer this. If I didn't answer it, I will try again.

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QUESTIONS BY MR. SNIDOW:
Q. Okay. Yeah, tell me.
Did you do this in your report?
A. Again, I'm not going to answer that question.
Q. Okay.
A. I'm going to describe to you what I did because you're asking me to respond to a single statement and it's taken out of context.
So I don't just look at a set of results and say, I don't believe there's consistency in this body of literature because there are differences in statistical significance. I say that weighs into my consideration, the Bradford Hill consideration, of overall consistency because the underlying data is inconsistent, in and of itself, in terms of how they're measuring things and what they're measuring.
And so you can't -- I can't -- maybe some people can. I can't isolate myself from the reality of the data and make a statement like that. I was pointing out the data in its own context.

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Q. Can you go to page 101 of your report?
A. I'm there.
Q. Can you find there where you told -- where you said what you just told me; that you've got to look at the underlying data when doing a consistency analysis?
MR. MURDICA: Objection to form.
THE WITNESS: So, again, this report --
QUESTIONS BY MR. SNIDOW:
Q. Just take a moment and tell me if it's there.
A. I can tell you that that's not in this section of the report.
Q. Okay.
A. This report was a review of the literature and an attempt to apply Bradford Hill where I didn't think it was necessary. And I'm using this chart as an example of one of the flaws in the underlying data, and that is part of my evaluation of inconsistency.
Q. All right. Okay. Let's go back to this chart.

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So here's the genetic confounding diagram. I want to walk through any evidence you have in support here.
There's no sibling-control study for autism, is there?
A. Not in this literature, there's not. There are many other sibling controls for autism, and I point them out in my literature because they're powerful ways to demonstrate and measure confounding.
Q. And Leppart showed no association here?
A. Leppart did not report an association for autism.
Q. And your theory is that there's a gene that's associated with autism and prenatal APAP use, right?
MR. MURDICA: Objection to form.
THE WITNESS: My theory is not that there's a gene. There is not a gene that causes autism. My theory is that there is a genetic predisposition that would increase a woman's willingness and need to use APAP

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during pregnancy.
It might be that she has depression or anxiety or can't sleep, and that is tied to her genes and, in turn, that genetic profile of the woman increases the risk of her having a child on the autism spectrum.
QUESTIONS BY MR. SNIDOW:
Q. That genetic profile has not been demonstrated to lead to increased use of ibuprofen; is that right?
MR. MURDICA: Objection to form.
THE WITNESS: So we know that women who are more anxious and who have more comorbid symptoms and who have more depression use more ibuprofen during pregnancy.
QUESTIONS BY MR. SNIDOW:
Q. Not my question.
Genetics. You have not been able to show the genetics association -- genetics associated with autism lead to increased use of ibuprofen; is that right?
A. So we don't know what the

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genetics are precisely that are associated with autism, and so we can't test that hypothesis.

What we can say is that because we know that autism is heritable, and we know that mothers are likely to have similar behaviors and characteristics, that that propensity to use more APAP is tied to their underlying anxiety, depression, neuroticism from the one study, et cetera.

Q. The genetics associated with autism have not been demonstrated to be associated with prepregnancy use of APAP; is that right?

MR. MURDICA: Objection to the form.

THE WITNESS: So there are some negative control studies that have attempted to look at prepregnancy use and post-pregnancy use, but, again, they are restricted to ADHD.

QUESTIONS BY MR. SNIDOW:

Q. So that's a no, right?

There's no study that shows that the genetics associated with autism lead

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to prepregnancy use?

A. We don't have a study to address that.

Q. And the same answer for post-pregnancy use; there's no study that shows the genetics associated with autism are associated with post-pregnancy use?

A. We don't have data to support that. It doesn't mean that it doesn't exist, but we don't have data to support it.

Q. Right.

Well, for ADHD we do have data, right?

A. Uh-huh.

Q. And so let's ask these questions here.

Genetics associated with ADHD, we have data suggesting that those are not associated with prepregnancy use, right?

A. I think we have data on both sides. We have some studies -- and I would need to pull them up and look at the exact citations, and some of it is in the supplementary material, but I'm happy to do that -- that actually shows an increased risk

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of ADHD among offspring for prepregnancy use and also for paternal use.

Q. Uh-huh. I know for paternal use.

Actually, can you walk me through that? You think that the paternal negative control is very instructive, right?

A. I think it's certainly important to try to use paternal use as a negative control in this --

Q. And you think it indicates confounding by genetics, don't you?

A. So if the paternal use prepregnancy confers an increased risk of autism, it's not an intrauterine effect. It means there's something else going on.

What that exactly is, I couldn't tell you because we don't understand all the genetics of autism. It could be a familial factor. It could be both familial and genetic, but it does point to residual confounding.

Q. But of genetics in particular is my question. Is that evidence of confounding by genetics or just something

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weird's going on?

MR. MURDICA: Objection to form.

THE WITNESS: Well, we don't know the genetics of autism. We don't know whether there is a paternal contribution and a maternal contribution. So we don't have the data to be able to test that specifically.

What we do have data on is to show that when you do that negative exposure control, the risk is there, which argues for confounding because --

MR. MURDICA: When you -- go ahead.

THE WITNESS: Sorry.

MR. MURDICA: No, I interrupted you. Continue.

THE WITNESS: You lost me.

MR. SNIDOW: Jim, were you going to ask me for a break?

MR. MURDICA: I was going to say it's been an hour, when it's a

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good point for you.
MR. SNIDOW: Now is good.
VIDEOGRAPHER: The time is 3:04 p.m., and we are off the record.
(Off the record at 3:04 p.m.)
VIDEOGRAPHER: The time is 3:18 p.m., and we're on the record.
QUESTIONS BY MR. SNIDOW:
Q. Could you turn to page -- to Exhibit 623, and it's going to be the page that's marked 426 maybe.
A. I'm sorry, what's -- so I have page --
MR. MURDICA: I think what they did is they appended a bunch of different excerpts together.
THE WITNESS: Oh, so it's way farther along? Got it. So I'm sorry, what number?
QUESTIONS BY MR. SNIDOW:
Q. 426.
A. Got it.
Q. And Jim is exactly right.
A. All right.
Q. Do you see where it says --

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MR. MURDICA: Can you read that back?
QUESTIONS BY MR. SNIDOW:
Q. Do you see where it says sibling-controls?
A. I do.
Q. It says, "Matching study subjects with siblings may be used in both cohort and case-control studies to control for shared genetic and environmental factors"?
A. I see that.
Q. And do you agree that it -- sibling controls do control both for genetic factors and for shared environmental factors?
A. So, yes. And I think the emphasis on shared environmental factors is important because it's critical that those environmental factors don't change from pregnancy to pregnancy, and there's times when they do.
Q. Yep.
If a sibling-controlled study did show statistically significant results, do you agree that would be compelling

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evidence that confounding by genetics is not the explanation?
MR. MURDICA: Objection to form.
THE WITNESS: If a sibling-control showed an effect, so even though it was not an intrauterine effect, you still saw effect -- an effect, that would point to genetics as a confounder.
QUESTIONS BY MR. SNIDOW:
Q. No, no, no.
A. I'm sorry, I didn't understand your --
Q. Yeah, that's okay.
A. -- hypothetical.
Q. All right. Here's the mom, right? She's got whatever genetics she has, right?
A. Okay.
Q. And then she's got two kids?
A. Right.
Q. And they can be boys, they can be girls, in the sibling studies. It doesn't matter, but she's got two kids. And one is

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exposed, and the other is not exposed.
This is how you do a sibling-control trial, right?
A. This is correct, right.
Q. And my question is, if the exposed child has an increased risk of the disease --
A. Uh-huh.
Q. -- that is compelling evidence that the mom's genetics is not confounding the association?
MR. MURDICA: Objection to form.
THE WITNESS: So the exposed child has an increased risk, and the unexposed child does not.
QUESTIONS BY MR. SNIDOW:
Q. Okay.
A. So that's your discordant pair right there.
Q. Yep.
A. So they're discordant on outcome, and they're discordant on exposure.
Q. Right.
A. And I would say that is

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evidence that genetics does not entirely explain the association, and that -- and yet, as we know, genetics is not everything. It's, you know -- heritability is not one.

And so it then has us look at what factors might explain the association.

Q. All I'm asking is, this would be strong evidence against genetic confounding?

MR. MURDICA: Objection to form.

THE WITNESS: Strong? I mean, I think it depends on the study, but it's evidence against genetic confounding, I'll give you that.

QUESTIONS BY MR. SNIDOW:

Q. Thank you.

In your report you cite von Ehrenstein as an example of a sibling-controlled study that I think you thought was done pretty well. It's on smoking.

MR. MURDICA: Objection to form.

THE WITNESS: Correct.

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(Pinto-Martin Exhibit 624 marked for identification.)

QUESTIONS BY MR. SNIDOW:

Q. And I'm going to show it to you. I'm going to mark this as 624, and it's tab R in case anyone cares. There you go.

All right. And this is von Ehrenstein, and they used a sibling-controlled study as a risk factor?

A. Uh-huh.

Q. And what they did was they found that heavy prenatal smoking was related to an odds ratio of, it looks like, 1.55 for autism?

A. Uh-huh.

Q. And that's their main analysis, right?

A. Again, I would want to look through and see, but that sounds right. That's usually what you quote in your abstracts, yeah.

Q. And that's going to be analogous when we look at it to the main Gustavson analysis?

A. Uh-huh.

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Q. Yeah.

Then it says, "In the sibling comparison, the odds ratio for heavy smoking was similarly elevated, but the confidence interval was wide"?

A. Uh-huh.

Q. And do you interpret that to mean was not statistically significant?

A. I don't know.

Q. We can look. Look at 733.

Do you see that there where they report the sibling controls?

A. I'm just studying it. Yep.

Q. Yeah.

And my question, so you know, is going to be no results across the board?

A. First -- within the sibling -- I'm sorry, I'm not understanding your question. Within the sibling cohort, there's no results across the board is what your statement is?

Q. Null results?

A. Oh, null results across the board.

Okay. I would say -- let's

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see. Null results throughout.

Q. All right. If you turn to page 731, the authors of this study say, "While the sibling comparison should adjust for shared familial factors by design, the approach has several limitations."

Do you agree with that?

MR. MURDICA: Object to the form.

THE WITNESS: I think there are -- again, this is a general statement, but I think there are problems with sibling controls. It's not a perfect measure of genetics.

It's probably as good as it gets, but, again, because we don't know all of the risk factors for something like autism spectrum disorders or ADHD, it's hard to know whether we are full -- fully controlling for everything.

QUESTIONS BY MR. SNIDOW:

Q. It says that they're prone to exposure misclassification?

A. Again, I'd want to understand

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why they're saying that, but that is a possibility in sibling controls.

Q. And exposure misclassifications when they're nondifferential bias results toward the null, right?

A. So in --

Q. That's just textbook, right?

A. In general, exposure misclassification, when it's not differential, reduces the measure of association.

Q. And that can lead to false negatives?

A. It can, and -- but I think it's important to understand the evidence that is behind that. Again, as I always say, it's not -- you can't -- that's a textbook definition, right? And then the context of the study and the measurement of exposure matters.

Q. Then it says, "Sibling-controlled studies usually have less power and generalizability."

Right?

A. Well, the less power is a

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function of what we talked about before, right? You are reducing down to siblings who are discordant on exposure and outcome. So that is going to reduce the study power by virtue of the sample size.

And less generalizability, I'd want to think about that. I'm sure exactly why they're saying that.

Q. Yeah, don't worry about that one. I just want to know about the power.

Sibling-controlled studies usually have less power, right?

A. Sibling-control studies usually have less power. I think that's --

Q. 732 on Ehren -- von Ehrenstein, at the top right -- top of the right-hand column, it says, "The sibling-comparison design are usually consistent with the findings from the full cohort. The small number of discordant siblings resulted in imprecise estimations, thus limiting our abilities to evaluate family-based confounding."

Right?

A. So what they're saying there is

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we're comparing the full cohort with the sibling discordant group and seeing if there's a difference.

And they're saying they're generally consistent with the full cohort, but where they're not, we're showing an intrauterine effect, and we're implicating genetics.

We have already talked about the limited sample size available to us, and of course the smaller the sample size, the less imprecise the estimates.

But, again, I will point out that even with a relatively limited sample size, Gustavson was able to demonstrate genetic confounding and to attenuate the association to the null.

Q. Okay. We'll get there.

You actually -- just you said -- you said of course the smaller the sample size, the less imprecise the estimates? I think you meant --

A. I'm sorry, I misspoke.

Q. Do you mind just saying it for me?

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A. So the smaller the sample size, the more likely we have imprecision in the estimate of the measure of association.

Q. And that can lead to false negatives?

MR. MURDICA: Objection to form.

THE WITNESS: It can lead to false negatives. It doesn't always lead to false negatives, right? And I think where we have a finding, we are showing that even a small sample can demonstrate a significant impact.

QUESTIONS BY MR. SNIDOW:

Q. Let's turn to 735. The von Ehrenstein authors say, "Sibling design has less statistical power and requires a relatively large number of discordant pairs."

A. I think I just said that.

Q. Yeah, I agree.

Then it says, "Thus sample size limitations did not allow us to assess the role of familial confounding as intended."

Right?

A. Uh-huh.

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Q. So what they're saying there is even though they got null results for the sibling-controlled studies, they're not sure whether that indicates genetic confounding or not, right?
A. So, again, that's a type 2 error, right? They're saying we don't have the power to really rule in or rule out, and that is different from saying we found an association that attenuated the full cohort.
Q. I don't know. Look at the table again. Look at Table 1.
A. I saw Table 1, but what --
Q. All right. So they got no results?
A. Right. But what they're saying -- read their sentence again.
Q. Uh-huh.
A. "The sibling design has less statistical power, requires a relatively large number of discordant pairs."
So they're saying we got a null result, but we're not sure that that wouldn't be different in if -- were we to have a large sample size.

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Right.
Q. Right. Yep.
And the sample size in von Ehrenstein, the number of discordant pairs was -- and you're going to have to help me here. It looks like discordant on --
A. Yeah, this is hard to do.
Q. Yeah. But I think discordant on both is 64.
A. I can spend some time, but I think so. Smoking during pregnancy.
Yeah, the maximum is 64. Yeah.
(Pinto-Martin Exhibit 625 marked for identification.)
QUESTIONS BY MR. SNIDOW:
Q. That's what I thought, too. Okay.
Then let's look at Frisell, which I think you cite as well, and I think you recently added it to your reliance list. I'm going to mark as 625. There you go.
You've seen this one before?
A. Uh-huh.
Q. And the title is "Invited commentary: Sibling-comparison designs, are

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they worth the effort?"
Right?
A. I have seen this.
Q. And you cite this in your paper?
A. I did.
Q. And if you turn to page 740, they start talking about von Ehrenstein.
A. Uh-huh.
Q. And they say, "If, on the other hand, an association remains, we have not shown that it's causal, but we have known that it is not entirely explained by confounding shared by the siblings."
I assume you fully agree?
A. Yes.
Q. It says, "It is thus imperative that we have sufficient power to demonstrate such a null finding."
A. Uh-huh.
Q. All right. They say that was the weakness in von Ehrenstein, right?
They say, "Only 58 of those were exposed to prenatal smoking, and many of them were likely from uninformative pairs."

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Correct?
MR. MURDICA: Object to the form.
THE WITNESS: So it's 58 who are discordant on exposure, so I think that our 64 guesstimate is incorrect.
QUESTIONS BY MR. SNIDOW:
Q. Yeah, I didn't get that either. But it's -- I didn't understand it.
A. It's less. It's --
Q. But they're saying it's 58, which is less.
A. 58 is dis -- discordant on exposure. Then you also have to say how many were discordant on outcome.
Q. Yeah.
A. So it's going to be much smaller, so it's -- you know, I don't know what it would be. Anyway, it's small.
Q. Yeah.
It says, "The results and broad confidence limits were consistent with both increased and decreased association compared with the full cohort."
Right?

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A. That's a hard sentence to understand, but that is what it says. In other words, they couldn't -- they couldn't rule out or rule in, yeah.
Q. All right. So they're saying based on the sample --
A. No association was possible, yeah.
Q. Based on the sample size in von Ehrenstein, they weren't able to say whether there was an actual increased or decreased association in the sibling-control part of the study.
A. Right.
Q. Is that right?
A. That's what they said, correct.
Q. Then it says, "Concluding remarks, sibling comparisons do indeed add unique value but only when the power is moderate to high."
A. Right.
Can we look at what they also say, which is, "Could we have foreseen this lack of power"? And they say, you know, "For binary exposure and outcome, it will be

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decided by the number of doubly discordant pairs," which is what we just talked about. "This, in turn, depends on the prevalence of exposure and outcome."
So they, too, are stating what I've been stating over and over again; that just relying on a statistical assessment of the ability to prove or disprove the null hypothesis is an imperfect way to do it, and you have to consider what you're measuring, how reliable that measure is, how prevalent that exposure is, et cetera.
Q. Okay. My question, though, do you see where they say "only when the power is moderate to high"?
A. I see that.
Q. And that's true; you need moderate to high power for sibling comparisons to have value?
A. And, again, you can't know that in advance, and it depends, as they just said, on the prevalence of the exposure. So that's one of the reasons they're so challenging, because you can't do a power analysis in advance, really.

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Q. Okay. Let's look at -- all right. Do you see the diagram?
A. Mom --
Q. Yeah.
A. -- discordant on exposure --
Q. Yeah.
A. -- and one child has autism, I think we're talking about here.
Is that right?
Q. Yeah.
A. Or ADHD?
Q. Yeah.
Brandlistuen found this for communication scores, externalizing behavior, internalizing behavior and higher activity levels, right?
A. Among the sibling control, Brandlistuen was able to show that the significant elevated effect remained. So arguing against an intrauterine effect.
However, I will point out that the screening tools that they used are not directly relevant to a diagnosis of ASD or ADHD, and they themselves in the paper call for a more refined analysis that's based on

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diagnostic outcome.
Q. And sorry, I think you misspoke again.
You said that argues against intrauterine effect. Did you mean argues against genetic confounding?
A. I'm sorry, yes.
Q. Is that right?
Just say it again. They found a result that argued against a genetic confounding?
A. They found a consistent effect among exposed and unexposed, which argues against the genetic effect.
Q. Thank you.
And --
A. However --
Q. Yeah, I get that it's not a -- it doesn't -- your point is it doesn't use ASD and ADHD clinical diagnoses of outcomes, right?
A. Right. These are -- these are screening outcomes that are not directly relevant to a diagnosis. And as I stated before, when we use a screening tool, it's to

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identify children in this case who might be at risk for a diagnosis. And so we set a very high sensitivity in order to get anyone who might be at risk, and we then subject them to further evaluation to determine the specific diagnosis.

I think it's really important to understand that in this literature.

Q. Okay. So this -- what I've drawn here, this is what Brandlistuen found?

A. Yeah. I'd like to pull it up and look specifically at the betas that they described, if we want to get into Brandlistuen, because the clinical significance of those findings is very questionable in my mind.

Q. That's all right.

A. You don't want to look at it?

Q. Not right now. I might later.

MR. SNIDOW: Actually, we'll you pull it out? Actually, can I see Brandlistuen? I'm not sure if we marked this one. You might be on a wild goose chase.

(Pinto-Martin Exhibit 626

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marked for identification.)

QUESTIONS BY MR. SNIDOW:

Q. All right. I'm going to mark it as 626. If we end up with two Brandlistuens, it's not the end of the world.

All right. This is what we were just talking about?

MR. MURDICA: Objection to form.

THE WITNESS: This is the Brandlistuen study.

QUESTIONS BY MR. SNIDOW:

Q. Turn to page 1711.

Do you see where it says, "A major strength in the study was the large sample size, enabling sibling-control design"?

A. I do see that.

Q. And if you look over here, since you wanted to talk about clinical terms, it says, "In clinical terms, these results suggest that exposure to paracetamol for more than 28 days during fetal life increases the risk of adverse psychomotor and behavioral outcomes by almost 70 percent and

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doubles the risk of language problems in 3-year-old children."

Did I read that correctly?

A. You read that correctly. That does not speak to the clinical significance of those findings with respect to a diagnostic outcome of ASD or ADHD.

Q. Well, then it does a comparison with smoking. It says, "For comparison, the effect of a well-established association between prenatal smoking and externalizing behavior problems has been reported to be as small as .07 in a recent study using sibling design."

Right?

A. Again, it does not speak to the clinical significance of this finding with respect to a diagnostic outcome, which is what I was evaluating in this literature.

Q. Again, what it's saying --

A. We see it in smoking, we see it in this, but it doesn't speak to the clinical significance, what is the construct validity of a communication problem with respect to ADHD or an externalizing behavior problem.

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Again, I would like to look at the size of those effects with respect to a diagnosis. We don't know.

Q. All right. While we're here, under the Discussion section on 1710, you see it says, "We found no association between ibuprofen on the same neurodevelopmental outcomes"?

A. I did -- I do see that.

Q. It says, "Which suggests a specific effect of paracetamol less likely to be confounded by indication"?

A. I do see that. Again, my earlier point about the paucity of ibuprofen consumption by pregnant women, because they're told not to take it, I think renders the comparison less than informative. And they had a yes/no measure of that exposure. It's just not compelling evidence in my mind.

Q. Brandlistuen had almost a thousand discordant pairs? If you look at 1704.

A. So they had 700 -- no, they had -- sorry, 805 who were discordant on exposure 1 to 27 days, and they had 134 who

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were discordant on greater than and equal to 28 days, which is what we're talking about.

But that does not address the -- the discordant on -- discordance on outcome, which, as we've said, are the only relevant pairs when you do the analysis. It doesn't tell us here how many were discordant on outcome, and it's because it's a regression analysis. It's not as easy to figure it out as when it's a matched, you know, sort of 2-by-2 table where you can look at the cells that actually contribute.

So --

Q. Based on this, can you say whether this was a large enough sibling-control study to give accurate results?

A. I can't, because I don't know the number of sibling discordant on these outcomes that they reported, and I couldn't find it anywhere in the paper.

Furthermore, as I've said repeatedly, the outcome is not relevant to my opinion about whether prenatal APAP is associated with ASD or ADHD.

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And so I think -- you know, I can't -- I can't make a judgment.

I will say one more thing that they also mention in their discussion of the results, which is that the MoBa cohort had a very high loss to follow-up. So the participant -- the participation rate was only about 40 percent, and what we know about participation in longitudinal cohort studies is that women with higher levels of anxiety are more likely to be retained in longitudinal studies, and we have a lot of good data supporting that.

Why? Because they're anxious, and they want to see what's happening with their child, and they want to bring their child back in for a checkup.

And so we have, at the end of the day, a highly selected population that have completed this series of long-term evaluations over time. Again, I think that's relevant to interpretation of the data.

Q. All right. Could you turn to page 7 of your report?

A. Hold on.

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7. Okay.

Q. Do you see in your report the sample size for Brandlistuen?

A. On page 7?

Q. Yep. I think so.

A. I'm not seeing it.

Q. No?

A. Here I'm talking about ecological studies on page 7. I start to talk about retrospective --

Q. Oh, sorry. You know what it is? It's page 7 of your appendix.

A. Okay. The appendix discussion? Okay.

Okay. So I have them -- so it's the first page of my appendix. Is that what we're looking at?

Q. Well, it's page 7 of your --

A. Well, it's page 27 in mine, so the numbering is different. Are you looking at the chart, or are you looking at the actual narrative?

Q. It says, "Appendices to Expert Report of Jennifer Pinto-Martin," and it should be page 7. It's a chart.

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A. Okay. So it's a chart. I'm sorry. I have both. I have a chart and a narrative.

Page 7, I'm there.

Q. All right. Do you see Brandlistuen?

A. I do.

Q. You report the sample size as the discordant pairs, right?

A. So that's what they reported, so that was all I was able to pull out of their paper --

Q. I'm not criticizing that.

A. -- that's 800-and-something discordant pairs.

Q. If you go to page 74 of your report.

A. Yep.

Q. You talk about Gustavson?

A. Gustavson 2021, yes.

Q. You report the population is 21,448?

A. Correct.

Q. You report the sibling-control result and the results?

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A. Uh-huh.
Q. But you never report the discordant pair numbers in your table here?
A. Not in the table, but in my overview of Gustavson in the narrative, I do.
Q. But you don't think you should -- I mean, I read this, and I said, wow, Gustavson had 21,000 people in the sibling control.
That's not accurate, right?
A. No, that's not accurate.
Q. Okay. Do you report any limitations for the Gustavson paper?
A. Well, certainly, because the Gustavson paper is based on the MoBa cohort, and that's not -- you know, as I said from the very beginning, that study was not designed to assess the relationship between APAP and neurodevelopmental outcome.
Q. Let's look at page 76 of your report.
MR. MURDICA: You interrupted her again.
MR. SNIDOW: I didn't mean to. I thought she was done.

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QUESTIONS BY MR. SNIDOW:
Q. All right. Can you go to 76 of your report?
A. I see, yeah.
Q. This is Gustavson?
A. Uh-huh.
Q. And where -- you just told me you reported the number of discordant pairs?
MR. MURDICA: Is that a question?
QUESTIONS BY MR. SNIDOW:
Q. Uh-huh.
Didn't you just tell me that your reported --
A. I did, and I thought I had reported it in my narrative. I do not see it, but I could cite it to you.
Q. That's a pretty important omission, right? Because that's the sample size that determines the power of that analysis, right?
MR. MURDICA: Objection to form.
THE WITNESS: That is the sample size that determines the power

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of that analysis. And as I've stated repeatedly, although there were only 34 discordant on both, the sibling then doubles that to 68, and at least 68 because there were additional siblings included in the analysis, and they found an attenuation of risk.
So when you find that a confounding estimate reduces the association to the null, the study power is not what you're worried about anymore. You've shown the association, and that's what we're after.
QUESTIONS BY MR. SNIDOW:
Q. Yeah.
But my question is this. For Brandlistuen, you noted the number of discordant pairs, right? Because that's what determines the power of the study, right?
Is that true?
A. I am surprised that I don't have the number for Gustavson in here because I truly thought I did. So if it was omitted, it was omitted in error. It was not an

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intentional omission.
Q. Okay. Well, do you report any limitations for Gustavson?
A. Again, when I describe the cohort in general, I do admit that the -- because the cohorts were not designed to measure this association, the possibility of recall bias with respect to exposure is always there.
Q. No, but there -- they're on that page. When you're describing Gustavson, do you ever say limitations of this study include, blah-blah-blah-blah-blah, like you do for everything else?
MR. MURDICA: Objection to form.
THE WITNESS: So Gustavson is the pinnacle of a series of studies that were done on the MoBa cohort, and when you understand how epidemiology involved -- evolved, you understand that, you know, irrespective of the methodologic challenges, investigators are trying to do a better and better job to demonstrate an association, and

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that's what's going on here.
QUESTIONS BY MR. SNIDOW:
Q. My question was, do you ever describe any limitations of the Gustavson study?
MR. MURDICA: Objection to form.
QUESTIONS BY MR. SNIDOW:
Q. Here, on page -- on page 76?
A. On page 76, I do not see any direct critique of the Gustavson paper.
Q. Do you agree that for many of the other studies, you provided extensive critiques of the studies?
MR. MURDICA: Objection to form.
THE WITNESS: So, again, I do agree with that, but can I just point out that because I describe many other studies from the MoBa cohort, I am stating the --
QUESTIONS BY MR. SNIDOW:
Q. And, ma'am, I'm not trying to be disrespectful. I just am trying to get an exhibit number.

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MR. MURDICA: Let the record reflect that Dr. Pinto-Martin is doing her best to answer the question and you're not paying attention, and you're having conversations and it's making it -- it's making it hard for me to defend it, it's making her -- hard for her to testify, and she just expressed that.
QUESTIONS BY MR. SNIDOW:
Q. Okay. I apologize. That wasn't my intention.
Could you look at --
A. Could I finish what I was saying?
Q. Well, sure. I didn't stop you.
A. What I do when I review a body of literature is discuss the study design for the cohort from which the data is derived, and I do that in many places in this report. It does not happen to appear on my discussion of Gustavson, which, as I said, is the latest study from a whole series that emerged from the MoBa cohort.
Q. Gustavson adds sibling controls

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to that body of literature, right?
A. It does.
Q. You don't report any limitations resulting from sibling-controlled analysis, right?
MR. MURDICA: Object to form.
QUESTIONS BY MR. SNIDOW:
Q. Any?
MR. MURDICA: Objection to the form.
THE WITNESS: To Gustavson sibling control?
QUESTIONS BY MR. SNIDOW:
Q. Correct.
A. I -- in this -- in this section right here, I do not critique Gustavson. I think it's a very important study. I obviously rely on it heavily because, as I pointed out repeatedly, the way epidemiology evolves is over time, with increased attention to detail and to addressing confounding. And only because the MoBa cohort continued to recruit siblings and had data on outcome was Gustavson able -- Gustavson and his coauthors, who prior had

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reported had an increased risk, were able to show that it was confounded by genetics because the cohort evolved and they had data on siblings.
Q. Can you look at Exhibit 605 for me?
A. 605 is what?
Q. It's the reference manual.
A. Okay. Hold on. Okay.
Q. Do you see where it says, "What's the power of the test?"
A. I'm sorry, what page are we looking at?
Q. 253.
A. Will you give me a page?
Q. Yes, that would have been a good -- that would've been a good thing to tell you. I agree.
A. 253. "What is the power of the test?"
Q. It says, "When a p-value is high, the findings are not significant, and the null hypothesis is not rejected."
True?
A. That's what it says.

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Q. And it says, "This could happen for at least two reasons," and let's turn the page.

The first is the null hypothesis is true, right?

A. Uh-huh.

Q. And that's what you think is going on in Gustavson, right?

A. I think it supports the notion of genetic confounding.

Q. And that's the null hypothesis that they're testing there essentially?

A. Well, they're testing confounding.

Q. Yeah.

A. So they're testing the impact of confounding on the prior association in the full cohort.

Q. But the second possibility is "the null is false, but by chance, the data happened to be of the kind expected under the null."

Did I read that correctly?

A. You did.

Q. And do you agree that is a

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possibility when study power is low?

A. I agree that it's a possibility when study power is low.

I think it's unlikely when you demonstrate such a significant decrease in the prior reported measure of association and it attenuates to the null with a small sample size that that possibility is likely.

Q. Then it says, "When a study with low power fails to show a significant effect," that's what happened in Gustavson, right?

MR. MURDICA: Object to the form.

THE WITNESS: So, again, the sibling analysis is embedded within the overall analysis. The sibling -- the study itself does not have low power.

It's like you're stratifying. If you think about it as stratifying, you're stratifying on the basis of genetics.

So the overall power of the study is the overall power of the

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study, and the sibling design is the stratification within that analysis.

QUESTIONS BY MR. SNIDOW:

Q. Do you see where it says, "The results may, therefore, be more fairly described as inconclusive than negative"?

A. I see that.

Q. All right. Do you agree with the statement that I've underlined here from the reference manual?

MR. MURDICA: Objection -- objection to form.

THE WITNESS: So, first of all, I don't know what this reference manual is. I don't know who wrote it. I don't know how it's used, and so I'm not going to agree or disagree with the statement that you've pulled out of it because I have no knowledge of its derivation.

QUESTIONS BY MR. SNIDOW:

Q. Okay. Do you agree when a study with low power fails to show a significant effect, the results may be more fairly described as inconclusive than

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negative?

Do you agree with that?

A. Again, you're asking me to agree with a statement that I have no knowledge of its purpose, its origin, who wrote it. I'm not willing to opine about random statements from manuals that I know nothing about.

Q. Okay. Can I ask you, you're a professor of epidemiology, right?

A. I am.

Q. And you all the time give your opinion about the basics of epidemiological technique, right?

A. I do, but that's not what I was asked --

Q. No, I know. I know.

A. -- to do here.

Q. I know.

A. And I'm not going to do it here. I think that textbooks can differ, manuals can differ, and I was here to -- I was asked here to evaluate the published epidemiologic literature, and I'm going to stay in that lane.

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Q. And you're telling me that in order to tell me whether this basic principle of epidemiology is true or false, you need to know who wrote it?

MR. MURDICA: Objection to the form.

THE WITNESS: I'm saying that my assignment here, if you will, was not to opine on statements about statistical significance and study power.

My assignment was to review the published epidemiologic literature, and I'm just going to stay there. This is not something I've ever seen before.

It's not -- I'm not opining as Jennifer Pinto-Martin, professor of epidemiology. I'm opining as an expert witness based on my review of the published literature, and that's what I am -- I'm here to talk about.

QUESTIONS BY MR. SNIDOW:

Q. Well, this isn't -- this isn't about APAP, right? This is -- this is about

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epidemiology. Can --

A. I recognize that.

Q. Can you answer the question? Is this -- is this true, or is this not true? Do you know?

A. I --

Q. Do you know if it's true or not?

MR. MURDICA: Objection. Objection to the form. Same objection.

THE WITNESS: Again, I'm not going to offer an opinion on a statement that was pulled randomly from a manual that I've never seen before, and it's not my assignment.

QUESTIONS BY MR. SNIDOW:

Q. Why does it matter who wrote it, like, truly? Why does it matter who wrote that?

What if a student came up to you and said, Dr. Pinto-Martin, when a study with low power fails to show a significant effect, the results may therefore be more fairly described as inclusive than negative,

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am I right or wrong, what would you tell them?

MR. MURDICA: Objection to form.

THE WITNESS: Again, hypothetical, I'm not going to respond to what I might say to a student in a different situation. That is not my role here.

QUESTIONS BY MR. SNIDOW:

Q. Right.

A. I'm not here as a professor of epidemiology. I'm here as an expert witness to review the published literature.

Q. Well, you're here as an expert in epidemiology, right?

A. I'm here as an expert epidemiologist who was asked to review the published literature.

(Pinto-Martin Exhibit 627 marked for identification.)

MR. SNIDOW: Could I have -- oh, yeah.

QUESTIONS BY MR. SNIDOW:

Q. Okay. All right. Doctor, this

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is what you've been wanting to do all day. We're going to look at Gustavson together.

MR. MURDICA: Objection to the commentary.

MR. SNIDOW: Harmless.

QUESTIONS BY MR. SNIDOW:

Q. 627.

All right. How would you characterize the statistical power of the main analysis, the non-sibling one, in Gustavson?

A. It's a very large cohort, and I think that statistical power is one important consideration in evaluating the integrity of the result that they present.

Q. High? Medium? Low?

MR. MURDICA: Objection. Form.

THE WITNESS: It's not a way that I typically evaluate statistical power, but it's a large study, as I said, and I think they had sufficient power to test the association that they were testing.

QUESTIONS BY MR. SNIDOW:

Q. Let's go to page 7.

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It looks like in the main analysis, the number of children not exposed to acetaminophen was 12,080?
A. Uh-huh.
Q. And you see that's what they're using as their control?
A. Yeah. It has the reference. Yeah.
Q. Yeah, the reference.
And then for acetaminophen, 29 days or more, it's 469?
A. Correct.
Q. So lower, but still pretty big, right?
A. It's 469.
Q. Yeah.
And they report an unadjusted and adjusted result. The unadjusted is 2.47; the adjusted is 2.02?
A. That's correct, that's what they state in this table.
Q. That corresponds to a doubling of the risk?
A. That is correct.
Q. Or 100 percent increase in

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risk?
A. That's what a twofold increase means, yes.
Q. And so I made a little diagram that I hope will illustrate this.
So this is the Gustavson primary analysis, right?
They looked at children not exposed to APAP. There were about 12,000 of them.
A. Uh-huh.
Q. Is that true? You gave me an "uh-huh."
Is that true?
A. That's true, uh-huh, so --
Q. Sorry, have to do that.
And then they looked at kids who were exposed to APAP for more than 29 days?
A. That's correct.
Q. And there were 469. And if you see here, I -- each one of these is going to represent 25 children.
A. Oh, I see. Okay.
Q. Okay?

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A. Got it.
Q. That's the setup for the Gustavson paper. It's a cohort study --
A. Uh-huh.
Q. -- prospective?
A. Prospective, although as I pointed out repeatedly, the assessment of exposure was actually retrospective because they were asking women during their pregnancy to recall exposure from the prior at least three months.
Q. Right.
But it wasn't retrospective after they learned whether or not they were going to experience the outcome, right?
A. They did not know the child's outcome at the time of assessment of exposure, correct.
Q. And for recall bias, that's typically what you're concerned about?
MR. MURDICA: Objection to form.
THE WITNESS: It's one reason that recall bias can be introduced. There are many other reasons,

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including, as I pointed out, the underlying psychological profile of the mother because we know that women with anxiety are more likely to remember negative events and report negative events.
QUESTIONS BY MR. SNIDOW:
Q. Yeah.
Well, let me ask you and -- while she's getting it. For the Gustavson paper, you agree only discordant siblings contribute with information in the sibling design?
A. That's correct.
Discordant on both.
Q. On both.
A. Doubly discordant, as we say.
Q. What did you say?
A. Doubly discordant.
(Pinto-Martin Exhibit 628 marked for identification.)
QUESTIONS BY MR. SNIDOW:
Q. Okay. I'm going to mark this as the Gustavson appendix. My tabs have disappeared yet again.

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MR. SNIDOW: What are we up to?
MS. BARRIERE: I'm checking. 628.
MR. SNIDOW: Okay. Thanks.
QUESTIONS BY MR. SNIDOW:
Q. This is the Gustavson supporting information. You've read this, right?
A. I have.
Q. And if you look at page 7, it says, "Only discordant siblings contribute with information in the sibling design."
True?
A. Correct.
Q. It says, "380 mothers participated with children discordant on the exposure for 29 days or more."
Right?
A. Sorry, you must have jumped. 300 -- okay.
Q. Yeah, I did. "380 mothers participated with children discordant on the exposure for 29 days or more."
A. Uh-huh.
Q. "34 of them have children

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discordant on the outcome."
A. Right.
Q. And then it looks like some of them have two, and then some of them have three?
A. Uh-huh. I think we end up with 38 or 39 by my calculation.
Q. Okay.
A. But then, of course, you need to double that.
Q. Right. Exactly.
A. Right?
Q. I was going to say, I went through this myself. I think -- I'm not 100 percent sure, but I think you'll agree with me that this is what the sample size looks like for the Gustavson sibling control because discordant on exposure was around 800 kids because 380 mothers.
MR. MURDICA: Objection to form.
QUESTIONS BY MR. SNIDOW:
Q. And discordant on ADHD diagnosis, I said about 72 because it looks like 36 times 2?

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MR. MURDICA: Objection to form and use of demonstrative.
THE WITNESS: So I'm sorry, but I believe that the 380 captures the discordance, so I don't think you need to double it.
QUESTIONS BY MR. SNIDOW:
Q. So you think actually --
A. See, they've already captured the discordance in that statement, so it's -- 380 are discordant on exposure.
Q. Well, it's mothers, isn't it?
A. Right.
Q. And they have kids. I -- that's why I said about --
A. No, but you measure it from the mother, right?
Q. Oh, okay.
A. Because the mom is the one who's exposed. So it's 380.
Q. Okay.
A. Or I think that's what it is, yeah.
Q. So it's smaller, smaller --
A. Greater than 29, and then

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you're right about sort of doubling the estimate of the discordant outcome.
Q. All right. So you think this is -- this is accurate on sample size for the Gustavson?
A. Close enough, yes.
Q. Yeah.
Agree, this is much smaller than this?
A. I agree that the sample size is small. Again, I will say the fact that a small sample was able to so effectively attenuate a prior reported association by the same authors -- so they're disagreeing with their prior finding.
They're actually debunking their prior finding, which is a very brave thing to do, but it happens in epidemiology because we want to get it right. We want to get to the truth, so we continue to analyze.
That's what they did here, and they were able to show genetics matters. They certainly point out that we want this replicated, but it is a very important finding in this -- in this arc of literature,

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it is a very important finding.
Q. Well, they said low sample size was a problem, didn't they?
MR. MURDICA: Objection to form.
THE WITNESS: They said that --
QUESTIONS BY MR. SNIDOW:
Q. Didn't they say that?
A. Let me quote what they said. "The results highlight the importance of using designs that allow for accounting for unmeasured confounding. As only discordant siblings contribute to information in sibling-control models, even the current very large birth cohort provided limit -- limited statistical power. Hence, the results need to be replicated."
So they acknowledged that it was limited statistical power, but they still found an association or an attenuation.
Q. Is your testimony they didn't say that the low power was a problem for those sibling controls?
MR. MURDICA: Objection to form.

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THE WITNESS: I just read you what they said.
QUESTIONS BY MR. SNIDOW.
Q. Well, let's look at the appendix.
A. I'm reading -- I'm -- okay.
Q. Yeah. Let's look at the appendix.
A. This is exactly what they say in their results.
Q. No. No. Hold on. Hold on.
Do you see this?
A. These numbers show that statistical power to detect within effects was relatively low.
Q. You agree?
A. But they found an effect.
Q. I -- I --
A. They're acknowledging that it was low, but they found an effect. And then they're saying, let's replicate this. How interesting.
They are calling for exactly what we do in epidemiology. Let's replicate this finding.

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Q. Hold on.
First of all, they found a null finding for the sibling controls, right? So I don't know what you mean by they found -- they found a null finding for the sibling controls.
A. So the purpose of the sibling control is to compare it to the main cohort analysis.
Q. Yep.
A. And they found an attenuation of the effect. That is an effect in my mind. It shows that there is confounding, which is the purpose of doing the sibling-control analysis.
Q. But you see here, "The numbers shows the statistical power to detect within effects was relatively low."
Did I read that correctly?
A. You did.
Q. All right. And then they say, "Hence, these results should be interpreted with caution."
Right?
A. A very -- a very wise thing to say.

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Q. You are not interpreting these results with caution, are you?
A. I am.
MR. MURDICA: Objection to form.
THE WITNESS: I'm saying they are incredibly interesting. They needed to be replicated.
Again, think about where they come in the arc of evidence, and this is very important to consider. This is the way epidemiology works.
I would love to see these results replicated, and I'm sure if anyone has the cohort to do it, they will do so.
QUESTIONS BY MR. SNIDOW:
Q. Yep.
This is -- when I asked you about ADHD -- I'm sorry. When I asked you about autism and ADHD, you said the sibling-control analysis were powerful evidence for you?
MR. MURDICA: Objection to

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form.
THE WITNESS: I'm sorry, I was --
QUESTIONS BY MR. SNIDOW:
Q. Yeah, you were -- when I asked you -- do remember about this?
A. Yes.
Q. Yeah.
A. Well, I said genetics is a powerful --
Q. And you said Gustavson --
A. -- factor.
Q. -- was your -- was your main basis; is that right?
A. For ADHD.
Q. For ADHD?
A. Right. I mean, that's the one that has a sibling control, so that's the only one you can look at.
Q. And they said, "Interpret our sibling control results with caution."
Right?
A. They didn't say ignore them. They said interpret them with caution. This is the first -- "We are the first group to do this" --
Q. Yes.
A. -- and they're putting it out there as a call for others to replicate, which is exactly what they should do.
Q. Yeah.
So let's look at page 8 of Gustavson.
A. Page 8 of Gustavson. Yeah, okay.
Q. Do you see, "This may lead to false conclusions that observed associations are due to familial confounding factors"?
Did I read that correctly?
MR. MURDICA: Objection to form.
THE WITNESS: So this -- let's go back and see what "this" is.
QUESTIONS BY MR. SNIDOW:
Q. Yeah, it's nondifferential misclassification error.
MR. MURDICA: Objection to form.
It's not a question.
THE WITNESS: It says,

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"Measurement error," which could mean lots of things, right? It could mean misclassification by exposure. It could mean imprecision in that exposure estimate.
"Measurement error" is a broad term. It's not -- they're not saying misclassification here. They're saying measurement error, and that's something that I pointed out repeatedly. We don't have solid exposure information from any of these data.
QUESTIONS BY MR. SNIDOW:
Q. But what they're saying here is that could lead to a false conclusion that the observed results are due to familial confounding factors.
A. That is what they're saying.
Q. Do you agree with that?
A. I think it's always a possibility in sibling control, but they're saying -- they have to be honest about what the results might mean. They're not dismissing their results on the basis of this. They're acknowledging that it -- that a sibling-control analysis has limitations, which I think is a very honest and straightforward way to do it.
And, by the way, did you notice one of the coauthors was the person that you were talking about earlier as a very renowned epidemiologist, the former department chair at Columbia, Ezra Susser, who I have great respect for.
I just point that out.
Q. So where in the Gustavson paper does it ever say, we have proven that these associations are the result of residual confounding?
MR. MURDICA: Objection to form.
THE WITNESS: So no credible epidemiologist would say they had proven anything on the basis of a single study.
What we do is analyze the data, put the data forth as evidence in support of the null hypothesis or in support of a research hypothesis and

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then call for confirmation of the finding.

And I think they were, again -- they showed a lot of integrity in the way that they presented their results.

QUESTIONS BY MR. SNIDOW:

Q. So that's a, no, they didn't say that.

MR. MURDICA: Objection to form.

THE WITNESS: I think I answered the question.

QUESTIONS BY MR. SNIDOW:

Q. Okay. Did they ever say, now that we have our sibling-control results, we know that the association between APAP and ADHD is a spurious one? Did they say that?

A. What they said was it points to evidence of confounding by genetics, and they called out for replication of the finding.

Again, that's precisely what I would expect an epidemiologist with integrity to do based on a single study.

Q. Let's look at the actual results of Gustavson and see how compelling

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they actually are.

So this is the table that they report?

A. Uh-huh.

Q. And this is the main result, right?

A. That is the result from the entire cohort.

Q. Yeah.

A. The model that was presented in Ystrom.

Q. And this is the sibling-control result that you like?

MR. MURDICA: Objection to form.

THE WITNESS: This is the result of the sibling-control analysis showing that the prior result is attenuated towards the null. You can see that the point estimate is down at 1, and it has a confidence interval that goes way below 1 and way above 1.

QUESTIONS BY MR. SNIDOW:

Q. It's actually 1.06, right?

A. I don't recall precisely, but

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that sounds right.

Q. So even in Gustavson, the child that was exposed to APAP in utero had a 6 -- the point estimate was a 6 percent higher risk of getting ADHD than his nonexposed -- his or her nonexposed sibling, right?

MR. MURDICA: Objection to form.

THE WITNESS: I don't think that's the way to interpret a sibling analysis. Because what a sibling analysis is designed to do is demonstrate the effect of genetic confounding. And so the result is the attenuation, the extent of attenuation, towards the null, which is very substantial, and the lack of statistical significance is also relevant here.

QUESTIONS BY MR. SNIDOW:

Q. Yeah. But I'm going to need an answer on this.

The actual results of the sibling control, the actual point estimate they got, showed that the exposed child had a

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6 percent higher likelihood of developing ADHD than the nonexposed sibling. That's what happened.

MR. MURDICA: Objection to form.

THE WITNESS: It's a not -- it's a nonsignificant finding, so I would never be willing to say that it illustrates a 6 percent increased risk.

It's -- it could have illustrated a result that is protective. It could have illustrated a result that was higher than that. So the point estimate is meaningless when you have wide confidence intervals and it's not significant.

QUESTIONS BY MR. SNIDOW:

Q. Exactly.

So it goes all the way up to, like, 2, right?

MR. MURDICA: Which one are you talking about now?

MR. SNIDOW: This one. It goes all the way up to 2.

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THE WITNESS: He's talking about more than 29 days, sibling control.

So the attenuation is towards the null, and the confidence intervals are wide, granted. But as I said, the interpretation is how does the sibling-controlled analysis -- this is -- this is the way you run the analysis, right. How does the sibling-control analysis compare to the full cohort analysis. And if we see that reduction in risk, it identifies genetics as a confounder.

Does it prove that this is all about genetics? No. And that's why they're saying, this is a really interesting finding, it shows the impact of genetics on that prior result, and we need more studies to do the same kind of thing.

QUESTIONS BY MR. SNIDOW:

Q. You think that when there are overlapping confidence intervals that raises the question of whether the values are

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meaningful different, right?

A. Sometimes. I -- I've said that, and I do think that sometimes, not always, but there are instances where it's pretty obvious that there's not a difference and someone is trying to describe it as different.

Q. This one, though, it's not that obvious, right? These confidence intervals are halfway overlapping, right?

A. Again, we're talking about two different analyses, and this is a subset of the prior analysis. So I don't think it's fair to talk about overlapping confidence intervals because we are doing basically a subanalysis, a stratified analysis from the overall cohort.

Q. I get that you don't think it's fair, but are these overlapping confidence intervals or not?

MR. MURDICA: Objection to form.

QUESTIONS BY MR. SNIDOW:

Q. Do they overlap?

MR. MURDICA: Objection to

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form.

THE WITNESS: You've already pointed out that they overlap --

QUESTIONS BY MR. SNIDOW:

Q. All right.

A. -- and I've tried to describe that I think when you're doing a sibling-control analysis, it's a subanalysis of your overall cohort. And comparing the width of the confidence intervals or the overlapping nature of the confidence intervals is not as relevant as it might be in a situation where you weren't doing a subanalysis within your overall cohort.

Q. Well, here's maybe why it could be relevant.

You can't statistically exclude the possibility that the main result was down here and the sibling-control result was up here, right?

MR. MURDICA: Objection to form.

QUESTIONS BY MR. SNIDOW:

Q. Can you exclude that statistically?

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A. So we know that the farther away you get from the point estimate on the confidence interval, the less likely that result is. I can't determine that looking at it right now, and they didn't try to determine that.

What they said was, our sibling-control analysis revealed evidence of confounding by genetics. We think that's important. There are many other people who have talked about the importance of genetic confounding. I would say almost every study that I reviewed said that in their conclusions and limitations, even if they found an effect, well, we need to be cautious in our interpretation because of the possibility of residual confounding by genetics.

So here we have a study that's actually able to demonstrate that it does have an impact.

Q. It says here, "Third, the sibling-comparison model adjusts not only for stable confounding factors but also for potential mediating factors"?

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A. That affect all siblings, that's correct.
Q. Yeah. You agree?
A. That is something that has been pointed out about sibling control, and it is an issue. In order to test for a mediation effect, you need to have what the mediator is, a definition of the mediator, and data on the mediator.
And I have -- I've seen nothing to support that the sibling-control analysis in this, or any other study that I've looked at, can demonstrate the impact of a mediating effect. It's theoretically possible. It's not what's happening here.
Q. But the authors call it out here, right?
A. Again, being honest, they say they have to note that this is -- you know, sibling-control analysis is a statistical technique. It's not perfect, but it has power in demonstrating the role of unmeasured confounding.
Q. Do you see here where they do their conclusions? You see where it says,

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"The results suggest that may be at least partly due to familial confounding"?
A. I do.
Q. Do you think it's all of it?
A. I don't think we can say on the basis of one study whether it's all of it or part of it. Again, without knowing what the components of familial confounding are, what we see is this has an impact, and we don't have the underlying data to really parse that.
Q. So you can't say for sure that genetic confounding explains the entire association between prenatal APAP exposure and autism?
MR. MURDICA: Objection to form.
THE WITNESS: I don't think anybody can. Because, again, autism is not completely heritable, and here we have a demonstration of a profound impact when we try to control for that heritability. But there's -- it's not a perfect measure, and it's one study.

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QUESTIONS BY MR. SNIDOW:
Q. And same question for ADHD. You can't say for sure that genetic confounding explains the entire association between prenatal APAP exposure and ADHD?
MR. MURDICA: Objection to form.
THE WITNESS: I cannot say that because we don't have evidence to support that. I think without, you know, designing a new study, there will always be the possibility of other confounders.
QUESTIONS BY MR. SNIDOW:
Q. And that's -- and that's a possibility, right?
Genetic confounding could be partially an explanation for the association, but there could remain some that's truly causal?
MR. MURDICA: Objection to form.
THE WITNESS: In my opinion, there is no evidence in the published literature, epidemiologic literature,

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to suggest a causal relationship.
There are many reasons for that. Genetic confounding is one of them, and all the other reasons we talked about all day long, which I can go through again, if you like, are the other reasons.
MR. SNIDOW: All right. Want to take a break?
THE WITNESS: Yes.
MR. MURDICA: Sure.
VIDEOGRAPHER: The time is 4:14 p.m., and we're off the record.
(Off the record at 4:14 p.m.)
VIDEOGRAPHER: The time is 4:26 p.m., and we're on the record.
MR. SNIDOW: Just for the record, based on Dr. Pinto's-Martin -- Pinto-Martin's refusal to answer my questions about whether statements about epidemiology in the reference manual were true or not, we are reserving the right to reopen the deposition.
MR. MURDICA: Regarding the

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one -- the one sentence you asked about?
MR. SNIDOW: That she told me she would not answer because it was not what she was called here to testify about.
MR. MURDICA: Okay. Why don't you just call the judge now?
MR. WATTS: Come on, guys. Let's go.
QUESTIONS BY MR. SNIDOW:
Q. All right. Dr. Pinto-Martin, do you agree that the work you do in the field of autism epidemiology relates to possible environmental causes?
A. I do.
Q. And that's work you do at UPenn?
A. That's correct.
Q. Part of your job duties at UPenn?
A. So it's a grant --
Q. Yeah.
A. -- right. So it's external funding to support research that is looking into the etiology of autism spectrum disorders.
Q. And on the Penn website you say that you're a researcher who looks into possible environmental causes of autism?
A. That's correct.
Q. And you agree that you were retained in this case in part because of your professional standing or expertise in the field of autism research?
MR. MURDICA: Objection to form.
THE WITNESS: I believe that's true.
QUESTIONS BY MR. SNIDOW:
Q. In particular, because of your professional standing or expertise in relation to potential environmental causes of autism?
MR. MURDICA: Objection to form.
THE WITNESS: I don't actually know. I mean, no one said to me, this is why we want to retain you.
I think that what you can see from my life's work, actually, is that I have devoted myself to understanding the etiology of autism spectrum disorders, and that includes potential environmental factors.
And, in fact, the SEED study that -- that the CDC has supported for many, many years now is looking at the genetic causes and the causes beyond genetics, I would say. Whatever -- however you want to characterize them.
QUESTIONS BY MR. SNIDOW:
Q. Okay. Do you agree that some of the associations in this literature are strong ones?
MR. MURDICA: Objection to the form.
THE WITNESS: So "strong" is a word that people use in epidemiology typically to describe the size of the measure of association. And so I ask you what you mean by "strong."
QUESTIONS BY MR. SNIDOW:
Q. You have a section in your report on strength. Okay?
So you have some idea of what you mean by strong or weak associations, right?
A. I do.
Q. Okay. So use that one, and tell me if some of the associations in the literature are strong.
A. So I would say that none of the associations in the literature are strong.
Q. All right.
A. Because although some of them report a measure of association that is some might say substantially above 1, the data supporting that measure of association is flawed and, therefore, I can't describe it as a strong association.
(Pinto-Martin Exhibit 629 marked for identification.)
QUESTIONS BY MR. SNIDOW:
Q. I'm going to show you a document that I'm going to mark as --
COURT REPORTER: 629.
MR. SNIDOW: Thank you.
QUESTIONS BY MR. SNIDOW:
Q. 629. It's the Ji 2020 paper.

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A. This one? Okay.
Q. Have you seen this one?
A. I have.
Q. And if you turn to page 186.
A. Uh-huh.
Q. They report the results, right?
A. They do.
Q. And you see for cord acetaminophen burden -- and that's their composite dataset?
A. Uh-huh.
Q. They report the results for ADHD?
A. They do.
Q. And for ASD?
A. Correct.
Q. The results for ADHD in the first -- excuse me, the second tertile is 2.26?
A. That's what they report.
Q. As compared to the first?
A. That's correct.
Q. 2.86 for the third?
A. That's correct.
Q. And those results are

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statistically significant?
A. They are significant, correct.
Q. That means less than 5 percent likelihood of being a chance finding there, right?
MR. MURDICA: Objection to form.
THE WITNESS: That's the definition of statistical significance, yes.
QUESTIONS BY MR. SNIDOW:
Q. For ASD, they report the odds ratio at 2.14?
A. For the second tertile, the odds ratio is 2.14, not statistically significant.
Q. 3.62 for the third?
A. Correct.
Q. And that one is?
A. And that one is statistically significant, yes.
Q. All right. Let's look at what that looks like.
So here is the results for Ji, right?

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MR. MURDICA: Objection to form and demonstrative.
THE WITNESS: So we have the first tertile. Clue me into your little diagram here.
So we have -- how many people do each -- does each little person represent on this one?
QUESTIONS BY MR. SNIDOW:
Q. It's in percent. So I've got 100 them.
A. Okay.
Q. And I've done percent. If you want to look --
A. No, it's okay.
Q. Yeah.
A. I just wanted to understand it.
Q. Yeah.
A. Okay. This is for ADHD, okay.
Q. And can you look at the cord acetaminophen burden table and tell me if I got this right?
A. We just went over the numbers, so, yes, you --
MR. MURDICA: Objection to the

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form and to the demonstrative that he created.
QUESTIONS BY MR. SNIDOW:
Q. It's -- did you say, Yeah, I got it right?
A. We just looked at those numbers, and these are consistent with what we just looked at.
Q. Yes.
MR. MURDICA: The doctor -- let the record reflect the doctor is looking at Exhibit 629, not whatever plaintiff's counsel created.
QUESTIONS BY MR. SNIDOW:
Q. Are you -- are you looking at this?
A. I'm looking at both.
Q. Okay. Good. I just wanted to make sure. Mr. Murdica suggested otherwise.
But -- so the second tertile here, a lot more kids got ADHD, would you agree?
MR. MURDICA: Objection to form.
THE WITNESS: A lot more kids

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is a pretty imprecise statement.
QUESTIONS BY MR. SNIDOW:
Q. All right. Well --
A. We can look at the exact number if we wanted to do that.
Q. More than a doubling of the risk?
A. It's more than a doubling of the risk, correct.
Q. And third tertile, 2.86?
A. Correct.
Q. That's more than doubling of the risk?
A. That's correct.
Q. All right. And the results here I'm reporting, those are adjusted results, true?
MR. MURDICA: Objection to form.
THE WITNESS: Those are adjusted by a set of potential confounders that include maternal age, race, ethnicity, education, marital status, stress during pregnancy, smoking before or during, alcohol

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before or during, maternal body mass index, parity, child sex, delivery type, preterm birth and low birth weight. Notably not genetics.
QUESTIONS BY MR. SNIDOW:
Q. Well, it's -- you can't just adjust for genetics, right? It's hard to measure.
A. Well, you could do a stratified analysis on --
Q. You can do things that are correlated with genetics, right?
A. That's what we've talked about.
Q. And sex is highly correlated with genetics?
A. It's determined by genetics.
Q. I agree.
Same thing with race, although obviously less than sex?
A. (Witness nods head.)
Q. Is that right?
MR. MURDICA: Objection to form.
THE WITNESS: I'm not sure the point of your question.

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QUESTIONS BY MR. SNIDOW:
Q. No, I'm just --
A. But, yes, that's true.
Q. My point is just that race is obviously correlated with genetics, right?
A. I would agree with that statement.
Q. And those were controlled in this study?
A. Those were controlled in that study.
Q. And did you notice in my -- in my diagram, I'm reporting essentially the crude risk ratios, right? Because I'm just showing the percentage of kids?
MR. MURDICA: Objection. Form.
THE WITNESS: You just told me you reported the adjusted, and that's what we are seeing here in this table.
QUESTIONS BY MR. SNIDOW:
Q. Well --
A. Cord acetaminophen --
Q. Well, I was actually trying to have you look at the percentages.
So you see the percentages.

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Remember I said I'm reporting percentages?
A. Well, you're showing the percentages with your little people.
Q. Uh-huh.
A. And you're reporting the relative risk that they report in their paper, which is what we do, right? We calculate the incidence in the exposed compared to the incidence in the unexposed, and that is how we get relative risk.
Q. Absolutely.
And so if I wanted to do the crude relative risk, I divide incidence here divided by here, right?
A. So --
MR. MURDICA: Objection to form.
THE WITNESS: So I wouldn't call it incidence because we don't know that these are incident cases. These are prevalent cases.
So we would look at the number of individuals with autism in one tertile compared to the reference tertile.

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QUESTIONS BY MR. SNIDOW:
Q. Yep.
Okay. What's it mean when you adjust for confounders and the association goes up versus the crude?
A. Very good question and very hard to interpret. We don't really know what that means. I mean, I think that it shows that there is something that we don't understand about the causal pathway is -- would be my first interpretation.
But it's a -- it's a challenging question that a lot of people have thought about, and I don't think there's a perfect answer for it.
Q. Okay. If we look at the chart for autism, you agree this is -- these are the results?
MR. MURDICA: Objection to form.
THE WITNESS: These are the results they report in Table 2, "adjusted associations between cord plasma acetaminophen biomarkers and the risk of physician-diagnosed

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conditions."
In this case, we're looking at ASD, and we looked before at ADHD.
I will say that the exposure information they're relying on here, cord acetaminophen burden and then various markers within that cord acetaminophen, is a point in time measurement that really only reflects exposure right around the time of delivery, and actually, perhaps, post-delivery for women who may have pain from a C-section or something like that.
So I think that it's important to point out what the tertiles reflect.
QUESTIONS BY MR. SNIDOW:
Q. All right. But these are the actual results?
A. These are the results reported in Table 2.
Q. All right. So kids who had more acetaminophen in their cord blood got more ASD than the ones who had less, right?

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A. The results indicate an increased risk among those who have cord acetaminophen measured right at the time of delivery, which is not relevant to fetal brain development throughout the trimesters.
So I question the value, I would say, of the results --
Q. Well --
A. -- with respect to informing my opinion about prenatal acetaminophen exposure and risk of ASD or ADHD.
Q. Well, the study authors didn't say it was worthless, right?
They said, "Our findings support previous studies regarding the association between prenatal and perinatal acetaminophen exposures and childhood neurodevelopmental risk"?
A. I mean, study authors rarely say that their findings are inconsequential.
Q. Right. I know.
A. I think they elsewhere talk about the notion that this is a point in time measurement and may not reflect anything other than perinatal exposure.

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Q. And that's a limitation, just like we saw in the Gustavson paper, right?
MR. MURDICA: Objection to form.
THE WITNESS: It's a rather -- it's a rather huge limitation in my mind when you're talking about fetal brain development, which starts very early on and continues throughout pregnancy.
And here we have an exposure that happened right at the end, and we're trying to link that to a diagnostic outcome.
QUESTIONS BY MR. SNIDOW:
Q. All right. They say, "The dose-response associations found for the current study also addressed the methodologic issues identified by the Society for Maternal -- Maternal-Fetal Medicine, FDA and American Association of Pediatrics regarding the reliance on maternal self-reported acetaminophen exposures in previous cohort studies."
Right?

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A. That's what they say.
Q. Right.
A. And I'm not sure I agree with that because the fact that they are relying on a biological marker may at first blush seem like a better approach to measuring exposure.
But if you think carefully about how fetal brain development works and how exposure in terms of dose and timing and duration might impact that, we have almost no information from this study on that.
Q. You see here they say, "Reliance on maternal self-reported"?
A. I see that.
Q. That's what you've been telling me about for a good amount of the day, right?
A. That is --
MR. MURDICA: Objection to form.
THE WITNESS: So maternal self-report is not a perfect measurement either.
QUESTIONS BY MR. SNIDOW:
Q. Yeah.

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A. What I'm saying is that these results, you pointed them out as the strongest results or big numbers.
And I'm just saying that they don't inform my opinion about prenatal use because I would say this is peripartum exposure and not prenatal.
Q. So you disagree with the authors' interpretation of their study, right?
A. I do.
Q. Or -- is that a "yes"?
A. I do.
Q. All right. They say they were dose-response patterns.
You disagree?
MR. MURDICA: Objection to form.
THE WITNESS: So I think that they have established that there's a dose-response by the biomarkers that they measure.
However, I don't know how those biomarkers related to fetal brain development, much less to the ultimate

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diagnosis of ASD or ADHD.
QUESTIONS BY MR. SNIDOW:
Q. Right.
Because no question, this is a dose-response, right?
MR. MURDICA: Objection to form.
THE WITNESS: Again, the biomarkers show an increased risk as the level of that biomarker goes up, but it was taken at the time of delivery and does not relate to fetal brain development, in my opinion.
QUESTIONS BY MR. SNIDOW:
Q. And, yeah. If you disagree, we'll just put it -- can I have Baker? Yep. Nope. Yeah.
All right. Did you review the Baker study?
A. I did.
Q. That one's about meconium?
A. Correct.
Q. And do you agree that the results in that were fairly strong?
MR. MURDICA: Objection to

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form.
THE WITNESS: I do not.
QUESTIONS BY MR. SNIDOW:
Q. All right. Well, while she's getting that, let me do one more thing.
Here's the secondhand smoke result. Do you remember that one?
A. I do.
Q. And here's the Baker result.
Do you see that?
A. I see that you've made a graphic of probably what comes from one of the tables.
Q. Yes.
A. So...
Q. So can you tell me which is a stronger association, this or this?
MR. MURDICA: Objection to form and the use of these graphics you created.
QUESTIONS BY MR. SNIDOW:
Q. Can you tell me that?
A. I can't tell you that because context matters.
Q. Yeah. That's fine.

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The number's a lot smaller, though, right? This one is 1.3, and this one is 3?

MR. MURDICA: Objection to form.

THE WITNESS: As I've said repeatedly, it's not just about the numbers.

QUESTIONS BY MR. SNIDOW:

Q. And can you give me a citation for that, that when you're looking for strength in Bradford Hill, you need to look at the underlying data and not just the magnitude of the association?

A. I can't cite you something specific to that, but I think it's a common belief among thoughtful epidemiologists that context is incredibly important.

Q. I know context is important, but we're doing strength.

Can you cite anything that says, you know, don't just look at the magnitude of the point estimate, you need to actually go and look at all of the data underlying all the studies?

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A. Again, I just think it's common sense. I don't look at things in isolation, so it's the way I approach things, and I'm not alone in that.

(Pinto-Martin Exhibit 630 marked for identification.)

QUESTIONS BY MR. SNIDOW:

Q. All right. Here is Baker, which Christy {sic} is going to tell me what to mark as.

A. 630, I think, right?

Q. Great. Here's Baker.

And do you see here they say, "A dose-response association was detected. Each doubling of exposure increased the odds of ADHD by 10 percent."

Do you see that?

A. I do see that.

Q. Do you agree that they detected a dose-response association here?

MR. MURDICA: Objection to form.

THE WITNESS: So the analytes from the meconium appear to increase the risk of the odds of ADHD.

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However, similar to the Ji study, I take exception to using a biomarker that is collected after delivery to reflect exposure throughout pregnancy.

Although we know that meconium does develop throughout pregnancy, we also know that babies don't poop, to be straightforward about it, until several days, sometimes, after delivery, and we know -- I'll just tell you because my mother -- my mother -- my daughter just had a baby, and she had a C-section, and so she was taking a lot of Tylenol after birth, and she was also nursing her baby.

And so I am quite sure that any acetaminophen that might have been detected in Teddy's poop could have been a function of the exposure she had during delivery, after delivery and through the breast milk.

QUESTIONS BY MR. SNIDOW:

Q. Right.

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Do you -- are you an expert in how exposures get into meconium at which points in pregnancy?

MR. MURDICA: Objection to form.

THE WITNESS: I'm not an expert in how exposures get into meconium during pregnancy, but I have read that exposures accumulate in meconium throughout pregnancy.

We have no information from Baker about how the exposure measured in the meconium relates to maternal usage throughout pregnancy.

QUESTIONS BY MR. SNIDOW:

Q. You see here, though, the conclusions they said, "By using a direct measurement of prenatal acetaminophen exposure that's unbiased by maternal recall."

Do you see that?

A. I do see that. And that's --

Q. Do you agree the measure was unbiased by maternal recall?

A. The measure is unbiased by maternal recall. That does not equate with

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demonstration of an increased risk of APAP in the meconium and ADHD or ASD.

Q. They seem to disagree. Because they said, "These results add evidence in support of the association between prenatal acetaminophen use and child ADHD."

Right?

MR. MURDICA: Objection to form.

THE WITNESS: That is their statement.

QUESTIONS BY MR. SNIDOW:

Q. Do you disagree with the study authors again?

A. I disagree with the study authors again.

Q. How many do you think you've disagreed with today? Do you think it's more than five?

MR. MURDICA: Objection to the form.

THE WITNESS: I didn't count.

QUESTIONS BY MR. SNIDOW:

Q. Well, what do you think is going on here? Why are all these

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researchers, who are doing this in their day job, getting all of this stuff wrong? Do you have an explanation for that?

MR. MURDICA: Objection to the form.

THE WITNESS: So I don't think it's a question of getting things wrong. I think these are people who are trying their best to understand whether there is a true causal association between prenatal APAP use and higher risk of an adverse neurodevelopmental outcome in the offspring.

Most epidemiologists, and I would put myself among them, care deeply about finding the truth. And so these are people who are doing their best with, as we've discussed, flawed data --

MS. BARRIERE: He's reading what you're saying at the same time.

MR. SNIDOW: Oh, yeah. Sorry about that. I got your transcript here.

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MS. BARRIERE: He's not ignoring you.

MR. SNIDOW: I've got to read what you're saying.

THE WITNESS: Okay. It's just very distracting to have you poking her and --

MR. SNIDOW: I couldn't -- I couldn't -- I couldn't see.

MS. BARRIERE: Sorry.

THE WITNESS: Okay. It's just -- I'm sorry. It's just distracting.

MR. SNIDOW: It's okay.

THE WITNESS: It feels disrespectful.

MS. BARRIERE: It wasn't intended.

MR. SNIDOW: It's really not. This is -- this is your transcript. I obviously have to read it. I can't look you in the eye and do that at the same time. I think you understand.

THE WITNESS: I didn't know that that's what you were doing.

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Thank you for explaining it.

QUESTIONS BY MR. SNIDOW:

Q. Yes. All right.

You want me to ask you the question again?

A. Yes, please.

Q. The people who keep saying, you know, we think this is -- this is causation, we don't think this is confounding and so on, what do you think is going on there?

MR. MURDICA: Objection to the form.

THE WITNESS: So what I think is going on is that epidemiologists who have data that might be relevant to the very important question of whether prenatal APAP exposure increases the risk of diagnostic ASD or ADHD are analyzing that data to the best of their ability and putting that information forth in the published literature.

And that has been going on for about ten years now pretty steadily, and the data is in toto not convincing

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because there are so many flaws.

It's a very, very difficult study to perform, in large part, because the exposure, which has to be precise with respect to timing and dose and duration, if we really want to know what its impact is on fetal brain development, is simply not there.

And these are two authors who've attempted to use a biological marker, but the biological marker itself has flaws with respect to interpreting timing, dose and duration.

QUESTIONS BY MR. SNIDOW:

Q. But you're not saying those authors are acting in bad faith?

A. Not at all.

Q. And you're not saying they're doing unreasonable science?

A. Not at all.

Q. And you're not saying that the methods that they've used to reach those conclusions are scientifically invalid ones,

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right?

A. No, I think -- as I said, I think everyone is doing their best job with all the data they have available, and all of these articles have gone through peer review, which means there are other scientists that agree, this is important information to put out there. But that's not the same thing as establishing a causal association.

Q. But including the papers that say, we think this strengthens the causal inference and so on, those went through peer review, right?

MR. MURDICA: Objection to form.

THE WITNESS: They did.

QUESTIONS BY MR. SNIDOW:

Q. And so you don't think that's an unreasonable thing to say, right?

A. I think --

MR. MURDICA: Objection to form.

Go ahead.

THE WITNESS: I think everybody is, again, trying to provide evidence

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that addresses the question of whether there is a true causal association, and I -- that's all I can say, is that people are doing the best with the data they have.

QUESTIONS BY MR. SNIDOW:

Q. And analyzing that data using scientifically reasonable means, right?

MR. MURDICA: Objection to form.

THE WITNESS: I think that these are scientifically reasonable means to address the question using the data that they have available. The data isn't perfect.

QUESTIONS BY MR. SNIDOW:

Q. Including the authors that you disagree with, right?

MR. MURDICA: Objection to form.

THE WITNESS: I'm not understanding that question.

QUESTIONS BY MR. SNIDOW:

Q. Yeah. The authors -- including the authors you disagree with on the

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causation question, confounding and so on, they're using scientifically reasonable means to address the data using imperfect data?

MR. MURDICA: Objection to form.

THE WITNESS: So they're using scientific means to address the question using imperfect data, and almost universally they're acknowledging the potential problems with drawing any causal conclusion from their data. Saying that something adds evidence or support is not the same as saying it causes.

QUESTIONS BY MR. SNIDOW:

Q. Do you see in Baker that they adjusted for hospital-administered acetaminophen?

A. I did see that.

Q. All right. And we were talking earlier about how when you're looking for a confounder and you adjust for it and the results don't change, that's evidence against the confounding?

MR. MURDICA: Objection to

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form.
THE WITNESS: Well, it suggests that the results are not confounded by that specific factor. It's not evidence against all confounding.
QUESTIONS BY MR. SNIDOW:
Q. And the specific factor was hospital-administered meconium? Hospital-administered --
A. I hope not.
Q. Yeah.
Hospital-administered APAP?
A. Sorry. Correct.
Q. Correct.
And that was the example you're giving about -- did you say your sis --
A. To my daughter.
Q. Your daughter. Okay.
That was the example you were giving, right?
A. Well, it was one example. She also took oral Tylenol or oral acetaminophen, whatever we -- I don't know exactly what the brand was, but she took it in the hospital in front of me and then proceeded to nurse her

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babies for several days before he had his first poop.
Q. And they adjusted for that in Baker?
MR. MURDICA: Objection to form.
THE WITNESS: Well, that's not injection. That's oral.
QUESTIONS BY MR. SNIDOW:
Q. No, but they adjusted for hospital-administered acetaminophen?
MR. MURDICA: Objection to form.
QUESTIONS BY MR. SNIDOW:
Q. And the results didn't change?
A. I need to look. I don't recall.
Q. Okay.
A. But irrespective of that, it doesn't change my evaluation of the contribution of this to the overall question of causation because of the issue of timing, dose and duration, which is just absent. We don't know throughout pregnancy how the -- women's use of acetaminophen correlates with

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the measure of meconium.
Q. Are you looking for that still?
MR. MURDICA: Objection to form.
THE WITNESS: I'm just seeing if I can find it, yeah.
I think it's probably in the supplements because I don't see it.
QUESTIONS BY MR. SNIDOW:
Q. All right. Don't worry about it.
Let me ask you this, though. If that's true, if they did adjust for hospital-administered acetaminophen, that would suggest that they're reporting results for acetaminophen that was taken during pregnancy, right?
MR. MURDICA: Objection to form.
THE WITNESS: I would like to see the exact numbers and how they adjusted for it. So it's hard for me to -- without seeing the numbers, it's hard for me to determine.

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QUESTIONS BY MR. SNIDOW:
Q. Okay. While we're looking for that, so you can see it, would you agree that results in Baker --
MR. MURDICA: He's asking you a question.
THE WITNESS: I'm sorry. I'm just trying to see if I could look in the supplementary materials in order to answer that question.
QUESTIONS BY MR. SNIDOW:
Q. It's all right. We'll dig it up. It will be faster.
Do you agree these --
A. I mean, I have it right in my binder. I can just look at it.
Q. Let me just find where it is in the table. I'm not -- I'll let you read it, I promise.
Do you see where it says "No acetaminophen" and "Yes acetaminophen"?
A. I see that, yes.
Q. And this is the first result in Baker. They did a yes/no comparison?
A. No acetaminophen and

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acetaminophen, yes.
Q. Did I accurately capture the results of Table 2?
A. You did, the adjusted analysis, the weighted -- the weighted analysis, I will say. That's what they call it.
Q. So in this study, the kids who had acetaminophen in their meconium had twice the likelihood of developing ADHD however many years later, right?
MR. MURDICA: Objection to the form.
THE WITNESS: The results support an increased risk of ADHD among children in whom meconium -- in whom APAP was detected in their meconium.
I'm really getting tired.
QUESTIONS BY MR. SNIDOW:
Q. Yeah.
And not just an increased risk, a doubling of the risk, right?
A. That's what they report in their study.
Q. And similarly here, they did a

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dose-response analysis, right?
MR. MURDICA: Objection to form. Use of the demonstrative.
Answer it, if you can.
THE WITNESS: So they used the levels in the meconium and characterized that as no, low or high. It's unclear to me exactly what that means. And then they looked to see whether the risk varied across those levels.
And in the low APAP, it appeared that there was not a significant risk. In the high APAP, it appeared that there was, with quite a substantially wide confidence interval.
QUESTIONS BY MR. SNIDOW:
Q. The risk ratio for high APAP use was 4.1?
A. That's what they report.
Q. That is a statistically significant result?
A. It is.
Q. The minimum they report in the

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confidence interval is 2.4?
A. Uh-huh.
Q. The point estimate suggests a 310 percent increase in the risk of ADHD?
A. That's correct.
Q. The high end of the confidence interval suggests a 609 -- sorry, a 595 percent increase in the risk of ADHD?
MR. MURDICA: Objection to form.
THE WITNESS: That's how we can interpret a confidence interval, yes.
QUESTIONS BY MR. SNIDOW:
Q. All right. And I imagine if I show you these again, you think that's stronger or weaker than the secondhand smoke result?
MR. MURDICA: Objection to form.
THE WITNESS: Again, I'm not going to compare across a completely different question and completely different exposure and a completely different outcome. It's not a fair comparison.

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QUESTIONS BY MR. SNIDOW:
Q. Well, this had a risk ratio of 1.3, I think we saw?
A. Again, we need to consider what the exposure is, how the exposure was measured, how reliable that is, what the outcome is. All of those things go into my evaluation. So just looking at the numbers is not a sufficient way to compare those two, in my mind.
Q. This risk ratio is 4?
A. We've said that this -- we've already established that, yes.
Q. And that's, what, hundreds of percent higher than the secondhand smoke one?
MR. MURDICA: Objection to form.
QUESTIONS BY MR. SNIDOW:
Q. Is that right?
A. Again, I'm not going to compare the results from a secondhand smoke study with very different exposure classification, measurement, precision, et cetera, to a study of meconium. It just doesn't -- it's not the way I would -- the way I do things.

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MR. SNIDOW: Jim, do you want to take a break and see what I can do to wrap up?
MR. MURDICA: Okay.
MR. SNIDOW: Thanks.
VIDEOGRAPHER: The time is 4:57 p.m., and we're off the record.
(Off the record at 4:57 p.m.)
VIDEOGRAPHER: The time is 5:11 p.m., and we're on the record.
QUESTIONS BY MR. SNIDOW:
Q. All right. Dr. Pinto-Martin, when assessing whether results in studies that report multiple results are statistically significant, are you familiar with a concept of a Bonferroni correction?
A. I am. I refer to it in my report.
Q. Yeah.
And what you do there is when you're reporting lots of results, that increases the likelihood of a chance finding, right?
A. That's correct.
Q. And I think the classic example

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is -- are you familiar with the study where they regress the zodiac signs on cardiac outcomes? No?
A. No, I'm not.
Q. Okay. You'll like this one. You should teach this one, too.
They found that two of the signs had statistically significant results as a matter of chance, and so you use it to illustrate why you got a Bonferroni correction.
Did you do a Bonferroni correction on any of the studies in the literature?
A. I did not. That was not part of what I was assigned to do. I was assigned to review the studies as they were published.
And so I certainly noted when I thought they should have done one and didn't, but I didn't conduct my own.
Q. Could you have done that?
A. Perhaps, if I'd had access to the data. It's hard to know whether you actually have access to the raw data in order to conduct something like that.

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Q. But that would have given you more information that -- as to whether or not there was a multiplicity issue, right?
A. Certainly. Doing the Bonferroni will tell you whether there's an issue there or not, but, again, without the raw data, that's just a hypothetical.
Q. Right.
But you didn't -- you didn't do one, did you?
A. I had no desire to do one, frankly. As I said, I reviewed the reported results from the authors and commented on those.
Q. Okay. Will you look at Baker again for me? It's the last one we were doing.
A. Yeah.
Q. Do you see here on page 1075 -- hold on a second.
A. Where are we? Yeah. 1075, yeah.
Q. You see above, "To explore potential dose-response association." It says, "In a sensitivity analysis, we excluded

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all mothers who were administered acetaminophen during delivery," right?
A. Uh-huh.
Q. It says, "To account for potential confounding by indication for use during labor"?
A. Uh-huh.
Q. All right. So they did a sensitivity analysis there, right?
A. Right. So a sensitivity analysis is a -- an attempt to control for something but not necessarily based on data.
And again, this is during labor. So I think we were talking about the hospital administration. That was your -- the term you used, and so I'm talking about oral administration post C-section. That's not during labor; it's post-labor.
So, you know, a woman can be given acetaminophen, and of course she will ask for it after a C-section because she's in pain, and then continue to take it during her stay in the hospital and before her baby's meconium is collected.
Q. But the baby at that point is

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out of the body?
A. The baby at that point is out of the body.
Q. And it's going into the baby via, in your theory, breast milk?
A. It's not a theory. It's -- we know that --
Q. Do they say that in Baker? I'm sorry, I didn't mean to interrupt you.
Do they say that in Baker?
MR. MURDICA: Hang on a second. You just -- you said you were sorry to interrupt her, and then you actually interrupted her.
You have let her answer the question before you ask a new one.
QUESTIONS BY MR. SNIDOW:
Q. Go ahead.
A. That's not something Baker addresses at all, which is why I think it's important to consider. He does not address the potential exposure through breastfeeding that would then result in an elevated level of acetaminophen in the meconium of the baby.

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QUESTIONS BY MR. SNIDOW:
Q. Do you have a paper or really any authority suggesting that a mother taking acetaminophen who is breastfeeding can end up in the meconium of the baby who's out of the body?
MR. MURDICA: Objection to form.
QUESTIONS BY MR. SNIDOW:
Q. Do you have a paper for that?
A. I don't have a paper for that.
Q. Okay.
A. I just know that that is a fact.
Q. Oh, you know it's a fact?
A. I know that I've heard it. I've read it. I don't know exactly where the information comes from, but meconium continues to accumulate exposures until it's released from the baby's body.
Q. And in your write-up of Baker in your report, did you say any of that?
MR. MURDICA: Objection to form.
THE WITNESS: Interestingly, I

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did not. My daughter hadn't had her baby yet, and I was struck by the fact that I was witnessing exactly what he was talking about because she was taking acetaminophen after pregnancy, she was nursing her baby.
And the meconium -- I wished I could have collected his meconium, in fact.
QUESTIONS BY MR. SNIDOW:
Q. Well, right.
But you weren't witnessing the acetaminophen go through the breast milk into the baby's meconium, right?
A. No, and --
MR. MURDICA: Objection to form.
QUESTIONS BY MR. SNIDOW:
Q. And you didn't talk about that at all in your report?
MR. MURDICA: Objection to form.
Which question do you want her to -- come on.

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QUESTIONS BY MR. SNIDOW:
Q. In your report --
MR. MURDICA: Ask a question.
QUESTIONS BY MR. SNIDOW:
Q. In your report, did you ever flag the possibility that a mother might introduce acetaminophen into the baby's meconium while breastfeeding and then that could have somehow messed up the Baker results?
MR. MURDICA: Asked and answered.
QUESTIONS BY MR. SNIDOW:
Q. Did you say that?
A. Again --
MR. MURDICA: Objection.
THE WITNESS: -- I said it was not a concept that I had thought about while -- when I was writing my report. It was something that occurred to me afterwards, so...
QUESTIONS BY MR. SNIDOW:
Q. When did your daughter have her baby?
A. The end of July.

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Q. All right. So in the past month, you could have updated your report, right?
MR. MURDICA: Objection to form.
THE WITNESS: I could have updated my report. I did not update my report. It's an anecdotal piece of evidence that I thought was worth pointing out.
QUESTIONS BY MR. SNIDOW:
Q. Yeah. It's -- it is anecdotal, true? Right?
MR. MURDICA: Objection to form.
QUESTIONS BY MR. SNIDOW:
Q. And do you typically rely on anecdotal evidence in your field?
MR. MURDICA: Objection to form.
THE WITNESS: I do not. I rely on published epidemiologic literature.
QUESTIONS BY MR. SNIDOW:
Q. Have you heard --
A. I just thought it was an

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interesting story.
Q. Well, I did, too, but now -- you're using it to undermine the published peer-reviewed study, so I've got to explore that.
A. I'm suggesting that it might have an impact. I think there are other reasons to -- and I've already stated them, to question the results of this study with respect to contributing to the evidence on causal association between acetaminophen and ADHD or ASD.
Q. Okay. Are you familiar with the max in your field, the plural of anecdote is not data?
MR. MURDICA: Objection to form.
THE WITNESS: I am.
QUESTIONS BY MR. SNIDOW:
Q. Do you agree with that one, by the way? I mean, isn't the plural of anecdote data?
MR. MURDICA: Objection to form.
THE WITNESS: I do not agree

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with that.
QUESTIONS BY MR. SNIDOW:
Q. Okay. All right. If the FDA said that the literature linking acetaminophen exposure to ADHD was consistent, would you disagree?
MR. MURDICA: Objection to form.
THE WITNESS: I'm sorry, I don't know what's happening.
MS. BARRIERE: I think we asked her a question.
QUESTIONS BY MR. SNIDOW:
Q. Oh, you said, I'm sorry, I don't know. I did not -- I did not hear you.
MR. MURDICA: No. I think this is all confused because you're looking over there and --
THE WITNESS: I don't know what's happening. Yeah.
MR. MURDICA: Why don't -- why don't you ask a new question.
QUESTIONS BY MR. SNIDOW:
Q. If the FDA said that literature linking acetaminophen exposure to ADHD was

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consistent, would you disagree?
A. So I would want to know where that statement was made and in what context and for what purpose. And again, I've described my definition of consistency, which I think incorporates things that others may not, including the FDA.
I don't -- I don't know, you know, the purpose of that -- of that statement by the FDA.
Q. Do you think you might agree?
MR. MURDICA: Objection to form.
THE WITNESS: I don't believe that this literature establishes a consistent association, so...
QUESTIONS BY MR. SNIDOW:
Q. Okay.
A. That's my finding.
(Pinto-Martin Exhibit 631 marked for identification.)
QUESTIONS BY MR. SNIDOW:
Q. All right. I'm going to mark 631, which is the Bradford Hill address.
Can you see if there's

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highlighting on that, Doctor?
A. It doesn't appear to have highlighting.
Q. Great.
Okay. Would you agree that the method laid out in the Bradford Hill address is considered the classic way to do causation analysis in your field?
MR. MURDICA: Objection. Form.
THE WITNESS: I think that the majority of epidemiologists use the Bradford Hill as a method of assessing a body of literature with respect to a causal association.
QUESTIONS BY MR. SNIDOW:
Q. You agree that's the right way to assess causation?
MR. MURDICA: Objection to form.
THE WITNESS: I don't know if I think it's right or wrong. It is what we use. It's -- it -- it's the established method. I don't know what you mean by "right," but it's the established method.

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QUESTIONS BY MR. SNIDOW:
Q. I don't know what the difference between that is either, but if you think it's the established, that's fine.
If you look here under Strength?
A. Uh-huh.
Q. Now, today you -- you've told me a few times that for strength, you need to look at the underlying data before you can determine whether a -- an association is strong or not, right?
A. So what I've tried to explain is that a strong association can still be flawed, and so you could have an odds ratio of 5, for example, or a relative risk of 5, that was either completely biased or confounded and, therefore, not representative of a strong association.
So taking the point estimate in isolation, in my mind, is an incomplete evaluation of strength.
Q. Okay. But can you tell me where in the Bradford Hill address it says you need to look at, like, how the exposure

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was gathered and some of the other stuff that you've mentioned today when deciding whether association is strong?
MR. MURDICA: Objection to form.
You can answer.
QUESTIONS BY MR. SNIDOW:
Q. Does it say to do that?
MR. MURDICA: Objection to form.
You answer it, you if you can.
THE WITNESS: The Bradford Hill criteria are a set of very simple statements about those criterion, and he does not tell us, you know, how to apply those to real world data that we are evaluating, much less a body of evidence that we are evaluating.
So that's my own expertise coming into play after years of reading studies, evaluating studies, understanding whether a purported association is strong just by virtue of its size or strong because it is meaningful in terms of the association

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that it represents.
QUESTIONS BY MR. SNIDOW:
Q. So that's a no. Bradford Hill doesn't say to go look at the underlying data?
MR. MURDICA: Objection to form.
QUESTIONS BY MR. SNIDOW:
Q. You can -- you can look.
A. Bradford Hill does not address how to apply the criteria. He describes the criteria and does not give us specific instructions about how to prioritize them or use them in an evaluation.
And I think that is the way that he wanted to put them out there, and then the utility of them has evolved over time.
Q. All right. So for consistency, he says, "Has it been repeatedly observed by different persons, in different places, circumstances and times"?
A. That's correct.
Q. And you'd agree that the association between APAP and ADHD and ASD has

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been observed by different persons, in different places, circumstances and times, right?

MR. MURDICA: Objection to form.

THE WITNESS: So observed is the relevant point here. I think there are studies that demonstrate that they have support for a causal association and studies that don't.

The consistency in terms of timing is all over the place, and the term -- the consistency in terms of dose is not there.

And so consistency, again, is considered in the context of the overall body of evidence, and in my mind, the consistency criteria is not met.

QUESTIONS BY MR. SNIDOW:

Q. Where does Bradford Hill say to consider really any of that? Dose? What else did you say? Time?

Does he say to do any of that?

MR. MURDICA: Objection to the

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form of the question.

THE WITNESS: As I said, he was laying out a set of criteria to be applied in the real world to a body of evidence, and I believe that the approach that I use is the correct approach for evaluating consistency and the other criteria.

QUESTIONS BY MR. SNIDOW:

Q. Well, I know you think it's right, but is that what Bradford Hill says? Can you find it here?

MR. MURDICA: Objection. You've now done this five times. I think that's enough, J.J.

MR. SNIDOW: Okay.

THE WITNESS: As I said, that was not what he did in this report. He was laying out the criteria for us to use in our evaluation in the real world.

QUESTIONS BY MR. SNIDOW:

Q. All right. Specificity is next. Agree that one is just very rarely satisfied, true?

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A. Depends on the body of evidence. Sometimes it's very nicely satisfied. It's certainly not satisfied in the APAP and neurodevelopmental outcome.

Q. It's certainly not satisfied in tobacco and lung cancer, right?

MR. MURDICA: Objection to form.

THE WITNESS: Again, there's examples where it's satisfied and examples where it's not.

I'm saying in this literature, it is clearly not satisfied.

QUESTIONS BY MR. SNIDOW:

Q. Right.

And Bradford Hill says that's okay, right?

He says, "If specificity exists, we may be able to draw conclusions without hesitation. If it's not apparent, we're not thereby necessarily left sitting irresolutely on the fence."

Right?

A. That's what it says.

Q. All right. Temporality, he

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says, that's about which is the cart and which is the horse, right?

A. Uh-huh.

Q. That's a statement about reverse causation?

MR. MURDICA: Objection to form.

THE WITNESS: That's --

QUESTIONS BY MR. SNIDOW:

Q. Yes?

A. -- part of what he's considering there, yes --

Q. Well --

A. -- in the criterion.

Q. That is what he's saying here, which is the cart, which is the horse; that's about reverse causation?

MR. MURDICA: Objection to form.

THE WITNESS: Well, it's about whether the exposure precedes the outcome, yeah.

QUESTIONS BY MR. SNIDOW:

Q. Does a particular diet lead to disease, or do the early stages of the

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disease lead to those particular diet particular habits. That's about reverse causation?

A. So it's about both, right. It's about, is there a causal pathway towards disease, or is the effect of the disease on the exposure what we're measuring here.

So he's saying both. He's saying it could be we see exposure to outcome, or it could be that the outcome is affecting the exposure. I think he's describing both.

Q. And in this literature here, you know, the way it kind of worked, was for the cohort study, take Liew 2016 as an example, they followed women, you know, kind of a time -- they followed them at time A, asked them about APAP use, waited ten years or so, and then looked at ADHD diagnoses?

A. So I'd like to know what specific study you're referring to. I'm pretty tired right now and just to throw something out like that, I'm not quite sure exactly what you're referring to.

But I can tell you about the

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methods of the study, if that's what you're asking about.

Q. Let me ask it a different way.

Do you think reverse causation is a possibility in this literature?

MR. MURDICA: Object to the form.

THE WITNESS: Can you describe what that reverse causation hypothesis would be?

QUESTIONS BY MR. SNIDOW:

Q. Sure.

Do you think that the child's diagnosis of ADHD could have caused the mother to take acetaminophen ten years earlier?

MR. MURDICA: Objection to form.

THE WITNESS: I think that that, as you presented it, is a highly unlikely scenario, but I do believe that maternal genetics can have an impact on the risk of a future child having autism.

So we know that autism is

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heritable, and we know that women who have one child with autism are more likely to have another child with autism. So her result in one pregnancy could affect her acetaminophen use and lots of other things in subsequent pregnancies.

QUESTIONS BY MR. SNIDOW:

Q. The strongest you'll give me on that is that it's highly unlikely that there's reverse causation?

MR. MURDICA: Objection to the -- to the form in which you're asking the question.

THE WITNESS: I'm not really understanding your question, quite frankly.

QUESTIONS BY MR. SNIDOW:

Q. All right. Here's how the studies work, right? The mother takes APAP, they wait a long time, they see whether the kid gets ADHD, right?

MR. MURDICA: Object to the form.

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QUESTIONS BY MR. SNIDOW:

Q. Is that basically right?

A. In some of those cohort studies, that's -- yeah.

Q. I'm asking you, is there any possibility that this caused that ten years earlier?

MR. MURDICA: Object to the form.

THE WITNESS: And I think I answered it. I don't think that that's likely. I think that the maternal genetic predisposition to having a child without -- with autism could affect a subsequent pregnancy.

QUESTIONS BY MR. SNIDOW:

Q. When you say it's not likely, I mean, is it possible? Does she have a time machine?

MR. MURDICA: Object to the form.

THE WITNESS: I think I've answered the question.

QUESTIONS BY MR. SNIDOW:

Q. Okay. But you're leaving open

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the possibility that this causes that, right?
A. No, I said --
MR. MURDICA: Object --
THE WITNESS: I mean, if you want me to say it in a more strong term, I will.
QUESTIONS BY MR. SNIDOW:
Q. Yes, please.
A. I don't think it's possible.
Q. All right. There you go.
All right.
A. Can I just point out that that's not the only thing that Bradford Hill was pointing out in that -- in that criterion?
Q. Okay. Biological gradient. That's dose-response?
A. That's correct.
Q. Okay. And what he says was, "For instance, the fact that the death rate from cancer of the lung rises linearly with the number of cigarettes smoked daily, adds a very great deal to the simpler evidence that cigarette smokers have a higher death rate than nonsmokers."

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Right?
A. That's correct.
Q. And you think that you need really good exposure data in order to be able to do that kind of analysis?
A. I certainly believe we need exposure data that is better than what we have in the APAP literature.
Q. And you think in 19 -- you think in 1965, they had, what, prescription databases for tobacco use?
A. I don't --
MR. MURDICA: Object to the form.
THE WITNESS: I don't believe they had prescription databases for tobacco use. It's, I would say, an easier proposition to describe the number of cigarettes you smoked per day, most people can -- back in the day would smoke a pack or more. So they often characterized it by packs and not just single cigarettes. So I just --

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QUESTIONS BY MR. SNIDOW:
Q. My point is this is self-reported data.
A. Perhaps. Perhaps. Perhaps it was counting cigarette butts. Perhaps it was partner exposure. I have no idea.
Q. You think -- you think that in the '50s and '60s that they had studies where they were counting cigarette butts to measure tobacco exposure?
MR. MURDICA: Object- -- objection to the form of the question.
THE WITNESS: I think it's possible.
QUESTIONS BY MR. SNIDOW:
Q. Now, where in Bradford Hill's analysis does he say to consider any of that? That you need really tight exposure data before you can do a dose-response analysis?
MR. MURDICA: Objection to form.
THE WITNESS: I think an epidemiologist with integrity would think very carefully about the basis for any purported association, and

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part of that would be looking at the integrity of the exposure information.
So he doesn't say it, as you -- as you've repeatedly pointed out, he doesn't contextualize, but I do. And I think contextualizing is absolutely essential when you're evaluating a body of literature.
QUESTIONS BY MR. SNIDOW:
Q. All right. Biological plausibility, right? You're not an expert in biological plausibility, are you?
MR. MURDICA: Objection to form.
We're really retreading ground here.
THE WITNESS: I am not.
QUESTIONS BY MR. SNIDOW:
Q. Okay. And then in your report you say that it's not -- that this association is not biologically plausible because they don't know for sure what the mechanism is, right?
A. The mechanism that they proposed -- the mechanisms that are proposed

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are all hypotheses, and we have no human data to support those hypotheses.

So, yes, we don't have that biological plausibility.

Q. Is there ever going to be human data on biological plausibility?

MR. MURDICA: Object to the form of the question.

THE WITNESS: I can't answer that question. I don't know. I don't know what the future will bring.

QUESTIONS BY MR. SNIDOW:

Q. Well, this is about how to go from observational studies to causation, right?

MR. MURDICA: Objection to form.

THE WITNESS: These are a set of criteria that we use to evaluate a body of evidence, which is what I did.

QUESTIONS BY MR. SNIDOW:

Q. And what does the word "plausible" mean?

A. Possible. I don't know what a synonym would be. Possible.

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Q. Possible.

A. Likely, maybe. Possibly likely. It's a little more than possible.

Q. You've read the literature that identified several potential causal pathways, right?

MR. MURDICA: Objection to form.

THE WITNESS: I have read the literature that hypothesizes causal mechanisms.

Again, I will repeat that there is no epidemiologic data to support any of those biological pathways.

QUESTIONS BY MR. SNIDOW:

Q. Coherence. And this is about having the epidemiologic data not seriously conflict with other known facts about the history of the disease, right?

A. That's what he says there, yes.

Q. And he says for tobacco, it's the fact that cigarette smoking was coherent with the temporal rise that has taken place over the -- in the two variables over the last generation, right?

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A. Right. And I think that that's an ecological assessment of using data that was much easier to acquire than what we are looking at here. Because of the changes in diagnostic criteria and awareness, as we know, that have had a profound impact on the prevalence of autism, it's very difficult for us to make the same kind of ecological argument.

Q. Well, but the skeptics said the same thing about tobacco, right? They said it was because of the development of X-rays and so on?

A. I don't know. I wasn't reading that literature back in the day.

Q. We looked at it just, like, two hours ago, right?

MR. MURDICA: Object to the form.

QUESTIONS BY MR. SNIDOW:

Q. Do you not remember?

MR. MURDICA: Objection.

THE WITNESS: Again, it's not something that I used to look at the evidence at APAP and

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neurodevelopmental outcome.

QUESTIONS BY MR. SNIDOW:

Q. Experiment. This one can be done with animal studies, right?

A. So there are experimental studies that attempt to characterize autism and ADHD in mice and rats. I don't believe that that's really a fair comparison because it's a bio -- it's a behaviorally based diagnosis.

Q. And then analogy. And that's when you look at other drugs that have been accepted as causal and see whether the mechanism is similar?

A. Correct.

Q. And you don't think that valproic acid is a good analogy?

MR. MURDICA: Object to the form.

And I think you're out of time. When you took an early break after only 25 minutes, I thought it was because you were going to end early; otherwise, I wouldn't have agreed to it. But I think we're done now.

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MR. SNIDOW: Okay. Can we do a time check?
VIDEOGRAPHER: 6 hours, 56 minutes.
MR. MURDICA: Okay.
MR. SNIDOW: Four minutes?
MR. MURDICA: Yeah. It's still amateur hour that you took an early break and then didn't end early.
But go ahead.
MR. SNIDOW: You did the exact same thing.
MR. MURDICA: I did not.
MR. SNIDOW: With Baccarelli. You took a break, like, ten minutes before you were done.
MR. MURDICA: Ten minutes before I was done. You took a break half an hour before you were done.
MR. SNIDOW: Oh. So that's how the pros do it.
MR. MURDICA: It was amateurish to take that break.
MR. SNIDOW: The pros do it -- the pros do it ten minutes before and

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not 30?
MR. MURDICA: That was amateurish.
Go ahead.
MR. SNIDOW: Okay.
THE WITNESS: So I do not believe that valproic acid is a legitimate analogy for all the reasons that I've described before, which include the fact that we have precise data on timing, dose and duration, precise data on indication of use.
QUESTIONS BY MR. SNIDOW:
Q. Okay. And then he says here, "None of my nine viewpoints can bring indisputable evidence for or against the cause-and-effect hypothesis."
Right?
A. He does say that.
Q. And you agree with that, right?
A. I do.
Q. And then he says, ultimately, that it's a matter of judgment, right? That there's no hard-and-fast rules for making the causation determination?

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A. That's correct. And that's what I believe, and that's what I've done in my application of the Bradford Hill.
Q. And he says, "The ultimate answer, though, is whether there's any other answer equally or more likely than cause and effect."
True?
A. That's correct.
Q. Okay.
A. And in my opinion, there is.
MR. SNIDOW: Okay. I'm going to, I think, pass the witness, Jim, but I've got some exhibits to mark.
And what number am I up to?
THE WITNESS: 631 is Baker, which I think is the last one you gave me. Or Bradford Hill, sorry.
MR. MURDICA: You're not marking the things you agreed not to mark, are you?
MR. SNIDOW: I am marking these. And you can talk to the judge or file a motion or whatever you want to do.

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MR. MURDICA: Well, you agreed not to mark them; otherwise, I said we would have talked to the judge then. And that's on the record.
So now that you're not marking these, they're not going to be part of the record, and the court reporter was here, and she knows what was said, and I'm going to ask the court reporter not to mark them.
MR. SNIDOW: Okay. Do you want to call the judge now to resolve this dispute?
MR. MURDICA: It's your -- it's your problem. You agreed not to do it. It's not my problem. It's your problem.
MR. SNIDOW: I'm not calling the judge. I'm just marking my exhibits.
MR. MURDICA: We are not going to have exhibits that were created by you. I made that very clear. And I said if there was any dispute over it, go to the judge then. I never would

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have allowed it to proceed if I knew you were going to walk back your agreement.

MR. SNIDOW: All right. Let's call the judge then.

MR. MURDICA: Yeah, call the judge.

MR. SNIDOW: No, I don't want to call the judge. I want to mark my exhibits.

MR. MURDICA: Well, it's your problem. They're not -- you agreed not to have them be exhibits. They're not going on the transcript.

MR. SNIDOW: Yeah. And I have some videos to mark, which I assume you'll object to.

MR. MURDICA: I think you should mark the entire thing, if you're going to mark a video.

MR. SNIDOW: That, I'm actually fine with, but it's going to take some time.

MR. MURDICA: Okay.

MR. SNIDOW: Do you want me to

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mark the whole thing?

MR. MURDICA: The videos?

MR. SNIDOW: Yeah.

MR. MURDICA: Yeah.

MR. SNIDOW: That, I can do.

MR. MURDICA: That would be the reasonable thing to do.

MR. SNIDOW: Okay.

MR. MURDICA: Just like not going back on an agreement.

MR. SNIDOW: And what I'm going to do is, I'll mark the snips, and then I'll mark the whole thing. So you'll have -- you can call them .1, .2, whatever. They're part of the full exhibit, but you'll have them.

All right?

MR. MURDICA: Sure.

Okay. So are we going to proceed now? You're not marking them, so --

MR. SNIDOW: I marked them.

MR. MURDICA: No, you didn't. You didn't.

MR. SNIDOW: Look, see.

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MR. MURDICA: You agreed not to. It's not -- it's not happening. That's totally unprofessional.

MR. SNIDOW: You can call the judge.

MR. MURDICA: They won't be part of the transcript because there was already an agreement in front of an officer of the court.

MR. SNIDOW: Yeah. You told me there was some rule against it; we looked into it, there's not, so...

MR. MURDICA: Look at what you said on the transcript and what I said.

MR. SNIDOW: You said that was against the rules --

MR. MURDICA: Okay. It doesn't matter. You agreed to it. It's not part of the record.

Okay. Let's continue.

MR. SNIDOW: Are you scared of them? Are you frightened of them? Why don't -- yeah. Why don't want them be part of the record? They were

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exhibits that we used with the witness.

MR. MURDICA: They're things that you created. They're things that you created. They're not accurate, and they're not appropriate exhibits. And that's why you agreed to not call the judge then when I told you you could have called the judge.

I'm not going to argue with you anymore. They're not exhibits. You agreed for them to not be exhibits, and you're not walking back an agreement. That's -- I mean, that's just pathetic.

All right.

MR. SNIDOW: You think that was respectful?

MR. MURDICA: I don't think it's respectful in the context of this litigation for you to make an agreement in the first hour of a deposition and then walk it back at the end of the deposition.

MR. SNIDOW: I really don't

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think I made an exhibit {sic}. I said -- all I said is I'll take it off. That's all I said. I didn't say I'm never marking these. I didn't say, oh, yeah, you're totally right. I said, I'll take it off.

MR. MURDICA: You can go read it and see if you -- see if that was a mootable of character.

(Pinto-Martin Exhibits 632, 633, 634, 635, 636, 637, 638, 639, 639.1, 639.2, 639.3, 639.4, 639.5, 639.6 and 639.7 marked for identification.)

CROSS-EXAMINATION

QUESTIONS BY MR. MURDICA:

Q. All right. Are you ready to proceed, Doctor?

A. Sure.

Q. All right. So let's make a note of when we're starting.

I'm just going to ask you a couple of questions about your examination today.

A. Okay.

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Q. Counsel for plaintiffs asked you about different confounding issues across the body of literature.

Do you remember that?

A. I do.

Q. Okay. And did the individual studies each have elements of confounding that were or were not accounted for?

A. Yes, and I tried to describe that. The set of confounders that the various cohort studies included vary, but they -- there are things that are included in some and not others, including, for example, maternal alcohol use and smoking, comorbid medical conditions, body mass index of the mother, stress during pregnancy, such things like that.

But, again, they vary in terms of which ones controlled for which, so I didn't want to try to make a general statement about it.

Q. You were asked questions about Exhibit 605, which is a Judicial Reference Manual?

A. Right, which I had never seen before, right.

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Q. And my question was going to be, have you ever seen that before?

A. No. I didn't -- I didn't know what it was for or where it came from. I tried to make that clear.

Q. Do you use that in your practice in any way?

A. No. As I said, I've never seen it before, and I don't know how it's used.

Q. Okay. And you were asked a bunch of questions on a particular sentence, I think it was from there, about whether a small sample size renders something inconclusive or actually negative.

A. Uh-huh.

Q. Do you remember those questions?

A. I do.

Q. And my question for you is this: Whether a study in the acetaminophen body of literature that you reviewed is inconclusive or negative, does it matter to your analysis -- your conclusion on causation here?

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A. It does not have an impact on my conclusion on cause -- causation.

Q. Why not?

A. Because my conclusion on causation is based on the body of evidence and all of the factors that we've described to date that are relevant to the methodologic issues within the literature.

Q. You were asked --

A. I think it's here. Are you looking for it?

Q. No. I'm looking for the next one, trying to save time here.

You were asked a question about Exhibit 615, the Ricci study.

Do you remember --

A. I do.

Q. -- seeing that earlier?

A. I do, yeah.

Q. And do you remember counsel asked you questions about negative meta-analyses? Remember that question?

A. Uh-huh.

Q. Okay. Was Ricci even able to do a meta-analysis on the autism data?

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A. No, and stated as much because of the heterogeneity of the studies.
Q. Okay. Do you recall being asked about Exhibit 609, which I'm putting in front of you, that is an Olsen and Liew study?
A. I do.
Q. And counsel went back to that a few times today if you recall.
Do you remember that?
A. Yes, I recall.
Q. Okay. And what was the year of that?
A. I believe it was 2016.
Q. And --
A. Yeah. 2017 it says here. Yeah.
Q. And counsel showed you that for his proposition that the confounders had -- that Liew allegedly thought the confounders had been accounted for.
Do you remember that?
A. That is what this opinion seems to indicate, yes.
Q. Okay. Have you seen, since you

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wrote your report, e-mails containing Dr. Liew's views on confounders that he wrote only three months ago?
A. I have.
Q. And what did you see Dr. Liew say about confounders?
A. That he was worried about genetic confounding. I don't know that he used the word "worry," concerned maybe, and that he noted that there had been a significant drop in the reported association once genetics were controlled for, and that he himself now had data, PRS data, that he was going to use to address the question of confounding by genetics.
Q. Okay. And have you seen that data published by Dr. Liew yet?
A. No, and as I've said, I would be anxious to see it.
Q. Okay. And did the DN -- did the Danish National Birth Cohort that he published his studies from have genetic data?
A. No, they did not control for genetic confounding.
Q. Okay. You were shown

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Exhibit 610 as well, which is the Gou study.
A. Uh-huh.
Q. Do you recall counsel showing you that as well earlier today?
A. I do.
Q. All right. And you were -- you were asked some questions about it, but I want to point you to something that counsel didn't show you or ask you about --
A. Okay.
Q. -- which is the second sentence of the conclusion, on page 205.
A. "Nevertheless, caution is advised when considering whether the association is causal because potentially unidentified or inadequately -- inadequately controlled confounding factors in the included studies may have unpredictable effects on the overall association."
And I have said that repeatedly. Like a meta-analysis is only as good as the data on which it relies, and we know that those data have potential confounders and biases.
Q. And that was right in

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Exhibit 610 that counsel asked you other questions about, right?
A. That's correct.
Q. Okay. You were asked a lot of questions about, you know, were the science -- you were asked a lot of questions about whether you disagreed with certain publication authors.
Do you remember those questions?
A. I do.
Q. And you were asked about whether, you know, they were trying hard, doing a good job, was it reasonable for them to publish their results.
Do you remember questions like that?
A. I do.
Q. Okay. For the conclusion that you made that the body of literature that you reviewed that was addressed here today does not support a causal relationship between in utero acetaminophen exposure and the outcomes of ADHD and/or autism, can reasonable epidemiologists disagree on that

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conclusion?
A. I don't think a reasonable epidemiologist could disagree with my conclusion based on this body of evidence that there is no cred -- credible support for a causal association between prenatal acetaminophen use and ASD or APAP -- ASD or ADHD.
And so the answer is no.
Q. Dr. Pinto-Martin, you issued a report, maybe at this point it's almost two months ago, right?
A. Yeah, end of June, I believe.
Q. Okay.
A. End of July.
Q. Since then, there's been numerous expert depositions of plaintiffs' experts and the defendants' experts, and the ones that have happened to date, have you reviewed their transcripts?
A. I have.
Q. Okay. Is there anything you've seen since you've issued your report, either in those deposition transcripts or from counsel today, that has changed your views

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and your conclusions in your report in any way?
A. Absolutely not.
MR. MURDICA: Okay. I don't have anything further.
MR. SNIDOW: Okay.
REDIRECT EXAMINATION
QUESTIONS BY MR. SNIDOW:
Q. Very briefly.
You mentioned some e-mails with Dr. Liew.
When did you look at those?
A. In the last two weeks, I would say.
Q. And it's your testimony that he said that genetic confounding was likely?
MR. MURDICA: Objection to the form.
THE WITNESS: I don't recall the specifics of the e-mail, but the gist of the message was that he had seen results where genetic confounding was illustrated, I'm imagining it was the Gustavson study, and was concerned about that as a potential confounder

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in this purported association, and that he himself was going to look at it in data that he now had that had PRS scores.
QUESTIONS BY MR. SNIDOW:
Q. But did he say that genetic confounding was likely in those e-mails?
MR. MURDICA: Objection. Objection to the form.
THE WITNESS: I don't believe I said that, and I don't believe -- I don't remember the specifics of the e-mail. I just looked at it and --
QUESTIONS BY MR. SNIDOW:
Q. Well, you talked about it with Mr. Murdica just now, right? You talked about those e-mails?
A. Not just now. I saw the e-mails back whenever they showed -- when the lawyers showed them to me. I read them. I don't -- I didn't retain that. I don't remember precisely what he said.
What I can say is that his -- the message that he was putting forth is a very different message from the opinion piece

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that you showed me, the Olsen and Liew piece.
And in addition, he's written another opinion piece, another commentary, that is also -- talks about the noncausal back door that can be opened if there's a genetic factor that both increases the use of APAP and increases the risk of ASD or ADHD.
So I just point it out because I think a thoughtful epidemiologist should consider that, and he is, and I hope he publishes on it.
Q. You said "and he is"?
MR. MURDICA: Objection.
THE WITNESS: Well, he says he's going to --
QUESTIONS BY MR. SNIDOW:
Q. No, he is a thoughtful epidemiologist?
A. If he -- if he proceeds with what he said he was going to do, which is to use new evidence to address prior associations that he's reported to see if there's confounding, I think that is a -- that shows integrity.
MR. SNIDOW: Okay. I have no

further questions.

MR. MURDICA: All right. Thank you.

VIDEOGRAPHER: The time is 5:48 p.m., and we are off the record.

(Deposition concluded at 5:48 p.m.)

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CERTIFICATE

I, CARRIE A. CAMPBELL, Registered Diplomate Reporter, Certified Realtime Reporter and Certified Shorthand Reporter, do hereby certify that prior to the commencement of the examination, Jennifer Pinto-Martin, Ph.D., MPH, was duly sworn by me to testify to the truth, the whole truth and nothing but the truth.

I DO FURTHER CERTIFY that the foregoing is a verbatim transcript of the testimony as taken stenographically by and before me at the time, place and on the date hereinbefore set forth, to the best of my ability.

I DO FURTHER CERTIFY that I am neither a relative nor employee nor attorney nor counsel of any of the parties to this action, and that I am neither a relative nor employee of such attorney or counsel, and that I am not financially interested in the action.

CARRIE A. CAMPBELL,
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Texas Certified Shorthand Reporter #9328
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Louisiana Certified Court Reporter #2021012
Notary Public
Dated: September 11, 2023

INSTRUCTIONS TO WITNESS

DATE: September 11, 2023

Please read your deposition over carefully and make any necessary corrections. You should state the reason in the appropriate space on the errata sheet for any corrections that are made.

After doing so, please sign the errata sheet and date it. You are signing same subject to the changes you have noted on the errata sheet, which will be attached to your deposition.

It is imperative that you return the original errata sheet to the deposing attorney within thirty (30) days of receipt of the deposition transcript by you. If you fail to do so, the deposition transcript may be deemed to be accurate and may be used in court.

ACKNOWLEDGMENT OF DEPONENT

I, _____, do hereby certify that I have read the foregoing pages and that the same is a correct transcription of the answers given by me to the questions therein propounded, except for the corrections or changes in form or substance, if any, noted in the attached Errata Sheet.

_____
Jennifer Pinto-Martin, Ph.D., MPH DATE

Subscribed and sworn to before me this _____ day of _____, 20 _____.

My commission expires: _____

Notary Public

ERRATA

PAGE	LINE	CHANGE

LAWYER'S NOTES

PAGE	LINE

WORD INDEX